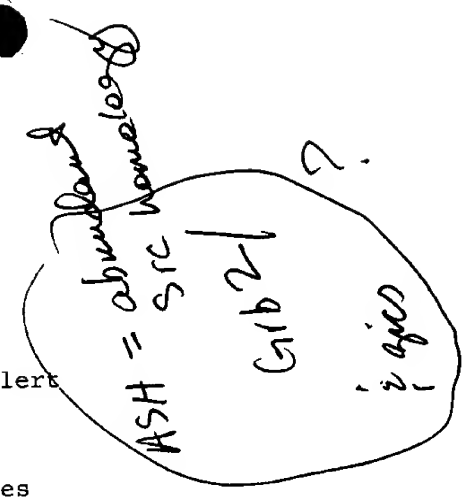


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feature enhanced with customized scheduling. See HELP ALERT.
  File   5:Biosis Previews(R)  1969-2002/Nov W1
         (c) 2002 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.

      Set  Items  Description
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      S2    7186  S1 AND CULTURE
? s s2 and transform
            7186  S2
           32767  TRANSFORM
      S3      19  S2 AND TRANSFORM
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? t s4/3,ab/all

 4/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13053630   21873646   PMID: 11881331
  [Neural stem cells in the brain]
  Stvolovaia nervnaia kletka mozga.
  Sosunov A A; Chelyshev Iu A
  Mordovian State University.
  Uspekhi fiziologicheskikh nauk (Russia)  Jan-Mar 2002,  33  (1)  p17-28,
ISSN 0301-1798   Journal Code: 0310750
  Document type: Journal Article; Review; Review, Academic ; English
Abstract
  Languages: RUSSIAN
  Main Citation Owner: NLM
  Record type: Completed
  Stem cells in the central nervous system were usually considered as
relevant for evaluation only in embryonic time. Recent advances in
molecular cloning and immunological identification of the different cell
types prove the presence of neurogenesis of the new neurons in adult
mammals brains. New neurons are born in two areas of the mammal and human
brain--sybventricular zone and subgranular zone of dentate gyrus. New born
granular neurons of dentate gyrus have a great importance for memory and
learning. New neurons originate from precursors which in culture and
in situ could also transform into astrocytes and oligodendrocytes,
thus fulfill criteria of neural stem cells. In culture, mitotic
activity of these stem sells depends on fibroblast growth factor 2 and
epidermal growth factor. Depletion of cultural medium of these factors and
addition of serum, other growth factors (Platelet-derived growth factor and
ciliary neurotrophic factor) leads to generation of neurons and astrocytes.
Isolation and clonal analysis of stem cells is based on immunological
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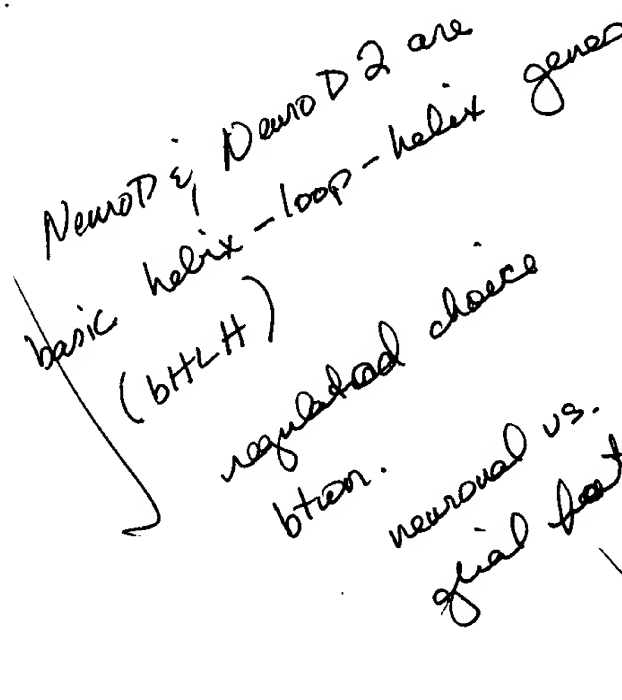

markers such as nestin, beta-tubulin III, some types of membrane glicoproteids. Identification and visualization of stem cells in brain revealed two populations of cells which have properties of stem cells. In embryonic time, radial glia cells could give origin to neurons, in mature brain cells expressing **glial** fibrillar acidic protein typical marker of astrocytes fulfill criteria for stem cells. Neural stem cells could **transform** not only into mature neurons and **glial** cells but also into blood cells, thus revealing broad spectrum of progenitors from different embryonic tissues. Further progress in this field of neurobiology could give prosperity in the cell therapy of many brain diseases.

4/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11259497 21286590 PMID: 11391706
In vitro model of microglial deramification: ramified microglia **transform** into amoeboid phagocytes following addition of brain cell membranes to microglia-astrocyte cocultures.
Bohatschek M; Kloss C U; Kalla R; Raivich G
Department of Neuromorphology, Max-Planck Institute for Neurobiology, Martinsried, Germany.
Journal of neuroscience research (United States) Jun 1 2001, 64 (5) p508-22, ISSN 0360-4012 Journal Code: 7600111
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Changes in the morphology of ramified microglia are a common feature in brain pathology and culminate in the appearance of small, rounded, microglia-derived phagocytes in the presence of neural debris. Here, we explored the effect of adding brain cell membranes on the morphology of alphaMbeta2-integrin (CD11b/CD18, CR3) positive microglia cultured on a confluent astrocyte substrate as an in vitro model of deramification. Addition of brain membranes led to a loss of microglial ramification, with full transformation to small, rounded, macrophages at 20-40 microg/ml. Time course studies showed a rapid response, with first effects at 1-3 hours, and full transformation at 24-48 hours. Removal of cell membranes and exchange of the **culture** medium led to a similarly rapid process of reramification. Comparison of cell membranes from different tissues at 20 microg/ml showed strong transforming effect for the brain, more moderate for kidney and liver, and very weak for spleen and skeletal muscle. Fluorescent labeling of brain membranes revealed uptake by almost all rounded macrophages, by a subpopulation of **glial** fibrillary acidic protein (GFAP)-positive astrocytes, but not by ramified microglia. Phagocytosis of inert fluorobeads did not lead to a transformation into macrophages but their phagocytosis was inhibited by brain membranes, pointing to a saturable uptake mechanism. In summary, addition of brain cell membranes and their phagocytosis leads to a rapid and reversible loss of ramification. The differences in transforming activity from different tissues and the absence of effect from phagocytosed fluorobeads suggest, however, the need for a second stimulus following the phagocytosis of cell debris. Copyright 2001 Wiley-Liss, Inc.

4/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10253125 99240648 PMID: 10222107
Mature astrocytes **transform** into transitional radial glia within adult mouse neocortex that supports directed migration of transplanted immature neurons.
Leavitt B R; Hernit-Grant C S; Macklis J D
Division of Neuroscience, Harvard Medical School and, Boston,

Massachusetts 02115, USA.
Experimental neurology (UNITED STATES) May 1999, 157 (1) p43-57,
ISSN 0014-4886 Journal Code: 0370712
Contract/Grant No.: HD18655; HD; NICHD; HD28478; HD; NICHD; NS07264; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Neuronal migration is an essential step in normal mammalian neocortical development, and the expression of defined cellular and molecular signals within the developing cortical microenvironment is likely crucial to this process. Therapy via transplanted or manipulated endogenous precursors for diseases which involve neuronal loss may depend critically on whether newly incorporated cells can actively migrate to repopulate areas of neuronal loss within the adult brain. Previous studies demonstrated that embryonic neurons and multipotent precursors transplanted into the neocortex of adult mice undergoing targeted apoptosis of pyramidal neurons migrate long distances into neuron-deficient regions, undergo directed differentiation, accept afferent synaptic input, and make appropriate long-distance projections. The experiments presented here: (1) use time-lapse digital confocal imaging of neuronal migration in living slice cultures to assess cellular mechanisms utilized by immature neurons during such long distance migration, and (2) identify changes within the host cortical astroglial population that may contribute to this migration. Prelabeled embryonic day 17 mouse neocortical neurons were transplanted into adult mouse primary somatosensory cortex undergoing targeted apoptotic degeneration of callosal projection neurons. Four to 7 days following transplantation, living slice cultures containing the region of transplanted cells were prepared and observed. Sequential time-lapse images were recorded using a video-based digital confocal microscope. Transplanted cells displayed bipolar morphologies characteristic of migrating neuroblasts and moved in a saltatory manner with mean rates of up to 14 microm/h. To investigate whether a permissive **glial** phenotype may provide a potential substrate for this directed form of neuronal migration, slice cultures were immunostained with the RC2 monoclonal antibody, which identifies radial glia that act as a substrate for neuronal migration during corticogenesis. RC2 does not label mature stellate astrocytes, which express **glial** fibrillary acidic protein (GFAP). RC2 expression was observed in **glial** cells closely apposed to migrating donor neurons within the slice cultures. The timing and specificity of RC2 expression was examined immunocytochemically at various times following transplantation. RC2 immunostaining within regions of neuronal degeneration was transient, with peak staining between 3 and 7 days following transplantation. Strongly RC2-immunoreactive cells that did not express GFAP were found within these regions, but not in distant cortical regions or within control brains. RC2-positive cells were identified in recipient transgenic mice which express beta-galactosidase under a **glial** specific promoter. Coexpression of RC2 and beta-galactosidase identified these cells as host astroglia. These results demonstrate that adult cortical astrocytes retain the capacity to reexpress an earlier developmental phenotype that may partially underlie the observed active migration of transplanted neurons and neural precursors. Further understanding of these processes could allow directed migration of transplanted or endogenous precursors toward therapeutic cellular repopulation and complex circuit reconstruction in neocortex and other CNS regions. Copyright 1999 Academic Press.

4/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09564517 97470287 PMID: 9329704
Support of homeostatic **glial** cell signaling: a novel therapeutic approach by propentofylline.

Schubert P; Ogata T; Rudolphi K; Marchini C; McRae A; Ferroni S
Max Planck-Institut fur Psychiatrie, Department of Neuromorphology, Martinsried, Germany.
Annals of the New York Academy of Sciences (UNITED STATES) Sep 26 1997, 826 p337-47, ISSN 0077-8923 Journal Code: 7506858
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A pathological **glial** cell activation, which forces microglia to **transform** into immunocompetent cells with cytotoxic properties and astrocytes to "de-differentiate," presumably adds to neurodegenerative diseases. We examined the modulatory effect of adenosine on the Ca2+ and cAMP-dependent regulation of such reactive **glial** cell properties in **culture** and tested possibilities of pharmacologic reinforcement. A strengthening of the cAMP-signaling, as could be achieved by adenosine agonists via a Ca(2+)-dependent action, favored the differentiation of proliferating astrocytes and associated neuroprotective properties (ion homeostasis, formation of trophic factors). But potentially neurotoxic properties of microglial cells were inhibited. Adenosine depressed their proliferation rate and transformation into macrophages, their particularly high formation of reactive oxygen intermediates and the release of the cytokine TNF-alpha. Similar effects were obtained with propentofylline, which acts as selective cAMP/cGMP phosphodiesterase inhibitor and also increases the effective concentration of adenosine by blocking its cellular reuptake. The recently observed induction of microglial apoptosis by elevated extracellular adenosine levels may further contribute to limit secondary nerve cell damage related to a pathological **glial** cell activation.

4/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08213521 94350462 PMID: 8070891
Development of microglia in mouse neopallial cell cultures.
Neuhaus J; Fedoroff S
Department of Anatomy, University of Saskatchewan, Saskatoon, Canada.
Glia (UNITED STATES) May 1994, 11 (1) p11-7, ISSN 0894-1491 Journal Code: 8806785
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Microglia develop in cultures initiated from disaggregated neopallial cells of newborn C3H/HeJ mice when the cultures are subjected to nutritional deprivation for 10 or more days (Hao et al: Int J Dev Neurosci 9:1-14, 1991). In the present experiments, the cultures were pulsed with BrdU for 3 hours at different times during incubation and then the cells were immunoreacted with antibodies against BrdU, GFAP, and CR3 receptor. The dividing cells (BrdU+) were found to be either GFAP+ or GFAP-, but not Mac-1+/BrdU+. Infection of proliferating cells after 2 or more days of incubation with replication-deficient retroviral vector containing E. coli lacZ reporter gene resulted in many labeled astroglia cell clones but no labeled microglia. However, when cells were infected right after disaggregation of neopallium, labeled Mac-1+ microglia were found. When Mac-1+ cells in a suspension of disaggregated neopallial cells were killed using complement mediated lysis before setting up the cultures, Mac-1+ microglia developed, in spite of the treatment. We conclude that in cultures initiated from mouse neopallium there are MAC-1-/GFAP- microglia progenitor cells which do not divide in nutritionally deprived cultures but can **transform** into Mac-1+ microglia under the influence of astroglia-derived trophic factors. Microglia, which become Mac-1+ (i.e., express CR3 receptor), proliferate extensively in the presence of CSF-1

(which is produced by astroglia).

4/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08036062 94170879 PMID: 8125159
Contrasting morphological changes in PC12 flat cells expressing two different forms of exogenous oncogenic ras.
Rozenberg Y Y; Howard B D
Department of Biological Chemistry, School of Medicine, University of California, Los Angeles 90024.
Experimental cell research (UNITED STATES) Mar 1994, 211 (1) p59-67, ISSN 0014-4827 Journal Code: 0373226
Contract/Grant No.: MH09736; MH; NIMH; MH38633; MH; NIMH
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Oncogenic ras is known to **transform** certain cells, whereas it induces terminal differentiation of others, e.g., neuronal differentiation of PC12 cells. MPT1 is a PC12 flat cell variant that extends **glial** -like processes and exhibits some properties of noncancer cells in **culture**, e.g., absence of anchorage-independent growth. Expression of oncogenic ras by MPT1 cells failed to result in neuronal differentiation, but such cells exhibited two contrasting morphological changes under certain conditions. First, they retained their extended processes in the presence of dexamethasone, unlike MPT1 cells not expressing oncogenic ras. Second, confluent cultures of ras-expressing MPT1 cells contained foci of transformed-looking cells that were refractile and grew in multiple layers. Thus, ras seemed to induce both a kind of differentiation and transformation of MPT1 cells. MPT1 cells were transfected with a plasmid carrying an oncogenic Harvey ras gene under transcriptional control of the metallothionein promoter. Two subclones of the transfected cells exhibited different responses to the induction of ras and expressed two different forms of the ras gene product. One clone extended dexamethasone-resistant processes and the second clone exhibited a more transformed phenotype. The ras gene product expressed in these two clones differed in migration on sodium dodecyl sulfate-polyacrylamide gel electrophoresis and in the extent of phosphorylation. These results suggest that ras protein phosphorylation may be important in determining whether a ras-mediated response is differentiation or transformation.

4/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07579015 93106299 PMID: 1468601
The 5 alpha-reductase in the brain: molecular aspects and relation to brain function.
Celotti F; Melcangi R C; Martini L
Department of Endocrinology, University of Milan, Italy.
Frontiers in neuroendocrinology (UNITED STATES) Apr 1992, 13 (2) p163-215, ISSN 0091-3022 Journal Code: 7513292
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
All the classes of hormonal steroids physiologically produced in the body (androgens, estrogens, progestagens, and corticosteroids) are able to exert important effects on the brain, but the mechanisms of their actions are not always well understood. Steroids may interact with intracellular receptors to activate the genome, but some of their effects are probably extragenomic and involve interactions with cellular membranes. Moreover, not all the

steroids act always in their native molecular form; a large group of them must actually be transformed into "active" metabolites. This may occur at the level of their respective target structures. For example, androgens are metabolized in the brain into estrogens and into 5 alpha-reduced androgens, like 5 alpha-androstan-17 beta-ol-3-one (dihydrotestosterone; DHT) and 5 alpha-androstan-3 alpha, 17 beta-diol (3 alpha-diol). Progesterone, and possibly corticosteroids, may also be transformed into their corresponding 5 alpha-reduced metabolites. Also the cellular target (neurons and/or **glial** cells) of the hormonal steroids in the brain is not always clear. This review analyzes in detail one of the two major enzymatic systems that **transform** steroids in the brain, namely the 5 alpha-reductase-3 alpha-(3 beta)-hydroxysteroid dehydrogenase pathway. An active 5 alpha-reductase-3 alpha-hydroxysteroid dehydrogenase system is widely distributed in practically all CNS structures in all phases of development. In the brain, this enzymatic system is not regulated by castration or sex steroid administration; furthermore, neural inputs seem to be ineffective at the hypothalamic level. A recent interesting finding is the presence of high concentrations of the 5 alpha-reductase in the white matter. This probably is due to the fact that the white matter is particularly rich in myelin membranes, with which the enzymatic activity appears to be associated. An active 5 alpha-reductase activity has also been shown to be present in peripheral myelinated nerves. The localization in myelin membranes may suggest a possible involvement of 5 alpha-reduced metabolites of the different steroids in the process of myelination. The presence of the 5 alpha-reductase was analyzed in neurons, astrocytes, and oligodendrocytes isolated from the brains of male rats, as well as in neurons and **glial** cells grown in **culture**. Neurons appear to be more active than **glial** cells in converting testosterone into DHT. Only neurons possess aromatase activity.(ABSTRACT TRUNCATED AT 400 WORDS)

4/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07374720 92309448 PMID: 1377283
Expression of the neu oncogene under the transcriptional control of the myelin basic protein gene in transgenic mice: generation of transformed **glial** cells.
Hayes C; Kelly D; Murayama S; Komiyama A; Suzuki K; Popko B
Brain and Development Research Center, University of North Carolina, Chapel Hill 27599-7250.
Journal of neuroscience research (UNITED STATES) Jan 1992, 31 (1) p175-87, ISSN 0360-4012 Journal Code: 7600111
Contract/Grant No.: ES 01104; ES; NIEHS; NS24453; NS; NINDS; R29 NS27336; NS; NINDS; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have taken a transgenic approach in an effort to specifically **transform** oligodendrocytes, the myelinating **glial** cells of the central nervous system (CNS). Transgenic mice were generated with a DNA construct that contained the activated neu oncogene under the transcriptional control of the myelin basic protein (MBP) gene. The MBP/c-neu transgenic animals have experienced a low incidence of brain tumors that express molecular markers specific to oligodendrocytes, providing a mouse model to study the formation and progression of oligodendrocyte tumors. A tumor from a transgenic animal has been dispersed in **culture** , and transformed cells that express properties of oligodendrocytes and astrocytes have been maintained. The degree to which these cells express phenotypic characteristic of oligodendrocytes or astrocytes is influenced by **culture** conditions. These transformed cells should serve as a valuable resource with which to study various molecular and biochemical aspects of the myelination process, as well as

the lineage interrelationship of CNS **glial** cells.

4/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05807283 88229710 PMID: 3259619
1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine metabolism and 1-methyl-4-phenylpyridinium uptake in dissociated cell cultures from the embryonic mesencephalon.
Schinelli S; Zuddas A; Kopin I J; Barker J L; di Porzio U
Section of Immunopharmacology, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20892.
Journal of neurochemistry (UNITED STATES) Jun 1988, 50 (6) p1900-7, ISSN 0022-3042 Journal Code: 2985190R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a contaminant found in a synthetic illicit drug, can elicit in humans and monkeys a severe extrapyramidal syndrome similar to Parkinson's disease. It also induces alterations of the dopamine (DA) pathways in rodents. MPTP neurotoxicity requires its enzymatic transformation into 1-methyl-4-phenylpyridinium (MPP+) by monoamine oxidase followed by its concentration into target cells, the DA neurons. Here, we show that mesencephalic **glial** cells from the mouse embryo can take up MPTP in vitro, **transform** it into MPP+, and release it into the **culture** medium. MPTP is not taken up by neurons from either the mesencephalon or the striatum in vitro (8 days in serum-free conditions). However, mesencephalic neurons in **culture** revealed a high-affinity uptake mechanism for the metabolite MPP+, similar to that for DA. The affinity (Km) for DA uptake is fivefold higher than that for MPP+ (0.2 and 1.1 microM, respectively), whereas the number of uptake sites for MPP+ is double (Vmax = 25 and 55 pmol/mg of protein/min for DA and MPP+, respectively). Mazindol, a DA uptake inhibitor, blocks the uptake of DA and MPP+ equally well under these conditions. Moreover, by competition experiments, the two molecules appear to use the same carrier(s) to enter DA neurons. Small concentrations of MPP+ are also taken up by striatal neurons in vitro. The amount taken up represented less than 10% of the MPP+ uptake in mesencephalic neurons. Depolarization induced by veratridine released comparable proportions of labeled DA and MPP+ from mesencephalic cultures. (ABSTRACT TRUNCATED AT 250 WORDS)

4/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05443865 87195043 PMID: 3571332
Neuronal inhibition of astroglial cell proliferation is membrane mediated.
Hatten M E
Journal of cell biology (UNITED STATES) May 1987, 104 (5) p1353-60, ISSN 0021-9525 Journal Code: 0375356
Contract/Grant No.: NS-15429; NS; NINDS; NS-21097; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Previously we have used a microwell tissue **culture** assay to show that early postnatal mouse cerebellar astroglia have a flattened morphology and proliferate rapidly when they are cultured in the absence of neurons, but develop specific cell-cell contacts and undergo morphological differentiation when they are co-cultured with purified granule neurons (Hatten, M. E., 1985, J. Cell Biol., 100:384-396). In these studies of cell

binding between neurons and astroglia, measurement with light and fluorescence microscopy or with [35S]methionine-labeled cells indicated that the kinetics of the binding of the neurons to astroglial cells are rapid, occurring within 10 min of the addition of the neurons to the growing glia. 6 h after neuronal attachment, astroglial DNA synthesis decreases, as shown by a two- to fivefold decrease in [3H]thymidine incorporation, and **glial** growth ceases. No effects on astroglial cell growth were seen after adding medium conditioned by purified cerebellar neurons cultured in the absence of astroglia, by astroglia cultured in the absence of neurons, or by a mixed population of cerebellar cells. This result was unchanged when any of these media were concentrated up to 50-fold, or when neurons and astroglia were cultured in separate chambers with confluent medium. Two groups of experiments suggest that membrane-membrane interactions between granule neurons and astroglia control astroglial cell growth. First, neurons fixed with dilute amounts of paraformaldehyde (0.5%) bound to the astroglia with the same kinetics as did living cells, inhibited DNA synthesis, and arrested **glial** growth within hours. Second, a cell membrane preparation of highly purified granule neurons also bound rapidly to the glia, decreased [3H]thymidine incorporation two- to fivefold and inhibited astroglial cell growth. The rate of the decrease in **glial** growth depended on the concentration of the granule neural membrane preparation added. A similar membrane preparation from purified cerebellar astroglial cells, PC12 cells, 3T3 mouse fibroblasts, or PTK rat epithelial cells did not decrease astroglial cell growth rates. Living neurons were the only preparation that both inhibited **glial** DNA synthesis and induced the astroglial cells to **transform** from the flat, epithelial shapes they have when they are cultured without neurons to highly differentiated forms that resemble Bergmann glia or astrocytes seen in vivo. These results suggest that membrane-membrane interactions between neurons and astroglia inhibit astroglial proliferation in vitro, and raise the possibility that membrane elements involved in **glial** growth regulation include neuron-**glial** interaction molecules.

4/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04975460 86052677 PMID: 4063824
Neoplastic transformation of newborn rat astrocytes in **culture**.
Bressler J P; de Vellis J
Brain research (NETHERLANDS) Nov 25 1985, 348 (1) p21-7, ISSN 0006-8993 Journal Code: 0045503
Contract/Grant No.: HD-06576; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A subpopulation of rat **glial** cells, derived from the astroglial population of newborn cerebral cortex cell cultures, spontaneously transformed in **culture** . Unlike the pretransformed cells, the transformed cells formed pile-up colonies, exhibited anchorage-independent growth, and were tumorigenic in young rats. Both the pretransformed and transformed cells exhibited differentiated properties characteristic of **glial** cells. For example, the pretransformed cells possessed hydrocortisone-inducible glutamine synthetase (GS), a property restricted to astrocytes in the central nervous system. As was anticipated, these cells did not exhibit either of two oligodendroglial characteristics, hydrocortisone-inducible glycerol phosphate dehydrogenase (GPDH) or the induction of lactate dehydrogenase (LDH) by N6,O6-dibutyryl cyclic adenosine 3':5'monophosphate (Bt2 cAMP). Unexpectedly, the transformed cells expressed the induction of glycerol phosphate dehydrogenase and lactate dehydrogenase but lost the glutamine synthetase induction. Both the pretransformed and transformed cells were examined ultrastructurally.

Neither cell type exhibited **glial** filaments (9-10 nm), a structure typical of astrocytes. Rather, the pretransformed cells were characterized by distinct longitudinal filaments near the cell surface and the absence of microtubules. On the other hand, the only cytoskeletal element visible in transformed cells were microtubules. Our work demonstrates that, like other rodent cell types, rat **glial** cells can spontaneously **transform** in **culture** . It also shows that the expression of differentiated properties are sensitive to the transformation process.

4/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04831411 85209946 PMID: 6543535
Astrocyte cell lineage. IV. Changes in the organization of microfilaments and adhesion patterns during astrocyte differentiation in **culture**.
Kalnins V I; Opas M; Ahmet I; Fedoroff S
Journal of neurocytology (ENGLAND) Dec 1984, 13 (6) p867-82, ISSN 0300-4864 Journal Code: 0364620
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The organization of microfilaments using NBD-phallacidin and cell adhesion to substratum by surface reflection interference microscopy was examined during differentiation of astrocytes in colony cultures and correlated with motile behaviour of cells. Disaggregated cells from neopallium of 12-day-old or newborn DBA/1J mouse embryos were used to establish colonies and astrocyte precursor cells at various stages of differentiation along the astrocyte lineage were examined after 3 days, 1, 2 and 4 weeks in **culture**. The earliest astrocyte precursor cells, the glioblasts, are stationary and form epithelial-type colonies which adhere to the substratum primarily around the edge where large microfilament bundles are found. Bundles of microfilaments are also present around the apical ends of closely packed cells. As the epithelial cells start to separate and **transform** into flat proastroblasts, adherens-type junctions which have a zig-zag appearance and are associated with microfilaments form between adjacent cells. In the highly motile astroblasts these junctional regions break down into multiple smaller regions where the separated cells remain in contact through fine processes. The astroblasts also have stress fibres, focal contacts with substratum, foci from which microfilament bundles radiate and a complex pattern of fine, circumferentially oriented bundles of microfilaments. This elaborate organization of microfilaments disappears as the motile astroblasts differentiate into stationary fibrous astrocytes that have little polymerized actin and lack focal contacts. These results show that stationary astrocyte precursor cells in vitro go through a highly motile stage having a characteristic distribution of microfilaments and focal contacts before becoming stationary again. We consider that the motile stage could correspond to the stage in vivo when astrocyte precursor cells migrate from the ventricular and subventricular regions to take up position in different parts of the developing brain.

4/3,AB/13 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13722727 BIOSIS NO.: 200200351548
Neural stem cell of brain.
AUTHOR: Sosunov A A(a); Chelyshev Yu A(a)
AUTHOR ADDRESS: (a)Mordovian State University, Kazan**Russia
JOURNAL: Uspekhi Fiziologicheskikh Nauk 33 (1):p17-28 January-March, 2002
MEDIUM: print

ISSN: 0301-1798
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: Russian; Non-English

ABSTRACT: Stem cells in the central nervous system were usually considered as relevant for evaluation only in embryonic time. Recent advances in molecular cloning and immunological identification of the different cell types prove the presence of neurogenesis of the new neurons in adult mammals brains. New neurons are born in two areas of the mammal and human brain - sybventricular zone and subgranular zone of dentate gyrus. New born granular neurons of dentate gyrus have a great importance for memory and learning. New neurons originate from precursors which in **culture** and in situ could also **transform** into astrocytes and oligodendrocytes, thus fulfil criteria of neural stem cells. In **culture**, mitotic activity of these stem sells depends on fibroblast growth factor 2 and epidermal growth factor. Depletion of cultural medium of these factors and addition of serum, other growth factors (Platelet-derived growth factor and ciliary neurotrophic factor) leads to generation of neurons and astrocytes. Isolation and clonal analysis of stem cells is based on immunological markers such as nestin, beta-tubulin III, some types of membrane glicoproteids. Identification and visualization of stem cells in brain revealed two polulations of cells which have properties of stem cells. In embryonic time, radial glia cells could give origin to neurons, in mature brain cells expressing **glial** fibrillar acidic pretein typical marker of astrocytes fulfil criteria for stem cells. Neural stem cells could **transform** not only into mature neurons and **glial** cells but also into blood cells, thus revealing broad spectrum of progenitors from different embryonic tissues. Further progress in this field of neurobiology could give prosperity in the cell therapy of many brain diseases.

2002

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Set     Items   Description
S1      60600   GLIAL
S2       7186   S1 AND CULTURE
S3         19   S2 AND TRANSFORM
S4         13   RD (unique items)
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          60600  S1
         597267  REVIEW
      S5    1250  S1 AND REVIEW
? s s5 and (neurod1 or neurod2 or ash1 or zic1 or zic2 or zic3 or myt1)
           1250  S5
             84  NEUROD1
             49  NEUROD2
            123  ASH1
             53  ZIC1
             67  ZIC2
             72  ZIC3
            108  MYT1
      S6       0  S5 AND (NEUROD1 OR NEUROD2 OR ASH1 OR ZIC1 OR ZIC2 OR
                  ZIC3 OR MYT1)
? s s5 and msx
           1250  S5
            830  MSX
      S7       0  S5 AND MSX
? s s5 and hes
           1250  S5
           2208  HES
      S8       0  S5 AND HES
? s s5 and epidermal and basal
           1250  S5
         117035  EPIDERMAL
         301830  BASAL
      S9       0  S5 AND EPIDERMAL AND BASAL
? s s1 and epidermal and basal
          60600  S1
         117035  EPIDERMAL
         301830  BASAL
     S10      59  S1 AND EPIDERMAL AND BASAL
? rd
...examined 50 records  (50)
...completed examining records
     S11      38  RD (unique items)
? t s11/3,ab/all

 11/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13799556   22227288   PMID: 12242309
  The neuron-specific Rai (ShcC) adaptor protein inhibits apoptosis by
coupling Ret to the phosphatidylinositol 3-kinase/Akt signaling pathway.
  Pelicci Giuliana; Troglio Flavia; Bodini Alessandra; Melillo Rosa Marina;
Pettirossi Valentina; Coda Laura; De Giuseppe Antonio; Santoro Massimo;
Pelicci Pier Giuseppe
  Department of Experimental Oncology, European Institute of Oncology,
20141 Milan, Italy. pgpelicci@ieo.it
  Molecular and cellular biology (United States) Oct 2002, 22 (20)
 p7351-63, ISSN 0270-7306  Journal Code: 8109087
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Rai is a recently identified member of the family of Shc-like proteins,
```

which are cytoplasmic signal transducers characterized by the unique PTB-CH1-SH2 modular organization. Rai expression is restricted to neuronal cells and regulates in vivo the number of postmitotic sympathetic neurons. We report here that Rai is not a common substrate of receptor tyrosine kinases under physiological conditions and that among the analyzed receptors (Ret, **epidermal** growth factor receptor, and TrkA) it is activated specifically by Ret. Overexpression of Rai in neuronal cell lines promoted survival by reducing apoptosis both under conditions of limited availability of the Ret ligand **glial** cell line-derived neurotrophic factor (GDNF) and in the absence of Ret activation. Overexpressed Rai resulted in the potentiation of the Ret-dependent activation of phosphatidylinositol 3-kinase (PI3K) and Akt. Notably, increased Akt phosphorylation and PI3K activity were also found under **basal** conditions, e.g., in serum-starved neuronal cells. Phosphorylated and hypophosphorylated Rai proteins form a constitutive complex with the p85 subunit of PI3K: upon Ret triggering, the Rai-PI3K complex is recruited to the tyrosine-phosphorylated Ret receptor through the binding of the Rai PTB domain to tyrosine 1062 of Ret. In neurons treated with low concentrations of GDNF, the prosurvival effect of Rai depends on Rai phosphorylation and Ret activation. In the absence of Ret activation, the prosurvival effect of Rai is, instead, phosphorylation independent. Finally, we showed that overexpression of Rai, at variance with Shc, had no effects on the early peak of mitogen-activated protein kinase (MAPK) activation, whereas it increased its activation at later time points. Phosphorylated Rai, however, was not found in complexes with Grb2. We propose that Rai potentiates the MAPK and PI3K signaling pathways and regulates Ret-dependent and -independent survival signals.

11/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13474045 22136176 PMID: 12140754
Elevated JNK activation contributes to the pathogenesis of human brain tumors.
Antonyak Marc A; Kenyon Lawrence C; Godwin Andrew K; James David C; Emlet David R; Okamoto Isamu; Tnani Mehdi; Holgado-Madruga Marina; Moscatello David K; Wong Albert J
The Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, Pennsylvania, PA 19107, USA.
Oncogene (England) Aug 1 2002, 21 (33) p5038-46, ISSN 0950-9232 Journal Code: 8711562
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The ERK pathway is typically associated with activation of the EGF receptor and has been shown to play a major role in promoting several tumor phenotypes. An analogous signaling module, the JNK pathway, has not been shown to be consistently activated by the EGF receptor but is instead more uniformly stimulated by cellular stresses and cytokines. The function of the JNK pathway in primary tumors is unclear as it has been implicated in both promoting apoptosis and cell growth in vitro, which may be a reflection of the cell lines chosen. Primary human brain tumors frequently show overexpression of the EGF receptor. To clarify the role of JNK in tumorigenesis, we have investigated the role of JNK in a large panel of primary human brain tumors and tumor derived cell lines. Here we present evidence that JNK has a major role in promoting tumorigenesis both in vivo and in vitro. Western blot analysis demonstrated that 86% (18 of 21) of primary brain tumors showed evidence of JNK activation but only 38% (8 of 21) showed evidence of ERK activation. Kinase assays revealed that 77% of brain tumor cell lines activated JNK in response to EGF (7 of 13) or had high levels of **basal** activity (3 of 13), whereas none of six normal cell lines analysed, including astrocytes, had these properties. Of several

growth factors examined, EGF produced the highest level of JNK induction in tumor cell lines and the duration of activation was greater than that seen for ERK. Expression of a dominant-negative (dn) form of JNK potently inhibited EGF mediated anchorage independent growth and protection from cell death in two **glial** tumor cell lines. These findings demonstrate that enhanced JNK activation is frequently found in primary brain tumors and that this activation contributes to phenotypes related to transformation.

11/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10955277 20532636 PMID: 11080176
Degradation of **glial** glutamate transporter mRNAs is selectively blocked by inhibition of cellular transcription.
Zelenaia O A; Robinson M B
Departments of Pediatrics and Pharmacology, Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia 19104-4318, USA.
Journal of neurochemistry (UNITED STATES) Dec 2000, 75 (6) p2252-8, ISSN 0022-3042 Journal Code: 2985190R
Contract/Grant No.: NS29869; NS; NINDS; NS36465; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Recent studies have demonstrated that the expression of the **glial** glutamate transporters GLT-1 (glutamate transporter 1) and GLAST (glutamate aspartate transporter) is regulated both in vivo and in vitro. For example, co-culturing with neurons, treatment with N:(6), 2'-O:-dibutyryladenosine 3':5'-cyclic monophosphate (dbcAMP), and treatment with **epidermal** growth factor all increase the steady-state levels of GLT-1 and GLAST protein in astrocyte cultures. These changes in protein expression are correlated with increased mRNA levels. In the present study, the degradation of GLT-1 and GLAST mRNAs was examined in control and dbcAMP-treated astrocyte cultures after inhibiting transcription with actinomycin D. Although one would predict that inhibition of transcription would cause a decrease in GLT-1 and GLAST mRNAs and that this decrease would depend on the rate of mRNA degradation, the levels of GLT-1 and GLAST mRNAs did not decrease even after 24 h of treatment with actinomycin D. Withdrawal of dbcAMP caused the levels of GLT-1 and GLAST mRNAs to fall to **basal** levels within 24 h, but this degradation was blocked if actinomycin D was added at the time of dbcAMP withdrawal. Importantly, actinomycin D did not block the degradation of c-fos mRNA also induced by dbcAMP in these cultures. Inhibition of translation with cycloheximide did not stabilize GLT-1 but partially attenuated the degradation of GLAST mRNA. Although the mechanism of this effect remains to be defined, these studies suggest that GLT-1 and GLAST mRNAs belong to a select class of inducible mRNAs stabilized by inhibitors of transcription. The possible relevance of these data to astrocyte differentiation is briefly discussed.

11/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10512170 20036196 PMID: 10571418
Differential control of VEGF synthesis and secretion in human glioma cells by IL-1 and EGF.
Valter M M; Wiestler O D; Pietsch T
University of Bonn, Department of Neuropathology, Germany. valter@biohp.harvard.edu
International journal of developmental neuroscience : the official journal of the International Society for Developmental Neuroscience (ENGLAND) Aug-Oct 1999, 17 (5-6) p565-77, ISSN 0736-5748

Journal Code: 8401784
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

VEGF (vascular endothelial growth factor), one of the most potent angiogenic factors, has recently been identified as an inducer of neoangiogenesis in many tumors including gliomas. VEGF itself appears to be regulated through different pathways. Since malignant gliomas frequently show EGF receptor amplification and express IL-1, a pivotal regulatory cytokine involved in angiogenesis, we analyzed interactions between EGF/EGF receptor and IL-1/IL-1 receptor and VEGF in the established glioblastoma cell lines U-87 MG and A-172. **Basal** VEGF expression was an order of magnitude higher in U-87 MG compared to A-172. IL-1 caused a fast and strong increase of VEGF secretion in U-87 MG which appeared to harbor an intracellular VEGF pool for enhanced exocytosis. The IL-1 receptor antagonist (IL-1-ra) reversed this effect suggesting an IL-1 receptor-associated mechanism. In contrast, VEGF secretion could not be increased by exogenous IL-1 exposure in A-172, which apparently lacked an intracellular VEGF pool for augmented exocytosis. However, IL-1-ra treatment alone caused a significant reduction of **basal** VEGF secretion in both U-87 MG and A-172. This suggests that baseline secretion of VEGF involves IL-1 receptor activation by endogenously produced IL-1. EGF also stimulated the secretion of VEGF into the cell supernatant. However, this effect, observed in both U-87 MG and A-172, was delayed and only occurred following replenishment of the intracellular VEGF pool. EGF upregulated the amount of VEGF mRNA. In general, the effects of IL-1 and EGF on VEGF were additive, suggesting independent mechanisms. Since IL-1 appears to be involved in VEGF secretion in **glial** tumors through an autocrine/paracrine mechanism, recombinant human IL-1-ra may evolve as a new agent for anti-angiogenic glioma therapy.

11/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10134491 99128470 PMID: 9929609
Generation of neurons from a nonneuronal precursor in adult olfactory epithelium in vitro.
Sicard G; Feron F; Andrieu J L; Holley A; Mackay-Sim A
Universite Claude Bernard, Villeurbanne, France.
Annals of the New York Academy of Sciences (UNITED STATES) Nov 30 1998, 855 p223-5, ISSN 0077-8923 Journal Code: 7506858
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Within the olfactory epithelium is a stem cell which can divide and differentiate to produce new sensory neurons. The identity of the neuronal stem cell is unknown but one candidate is the horizontal **basal** cell which lies adjacent to the basement membrane and expresses keratin. Previous attempts to generate mature sensory neurons from purified horizontal **basal** cells in vitro were unsuccessful. We show here for the first time that olfactory neurogenesis can be reproduced in vitro from partially-purified cultures of adult rat precursor cells cultivated in a serum-free medium. Rat olfactory epithelium was dissected from the nasal septum and separated from the underlying lamina propria, and its cells were dissociated and grown in a medium containing **epidermal** growth factor for 5 days. Immunochemistry showed that only supporting cells (SUS1-positive) and horizontal **basal** cells (keratin-positive) survived for this period. At day 6, the cells were stressed either by passaging them or by a simple mechanical stress. In each case, a morphological and immunological differentiation was observed within 24-48 hr. Newly formed bipolar cells were found to be S100-, **glial**

fibrillary acidic protein (GFAP-), neural cell adhesion molecule (N-CAM+), and/or microtubule-associated protein 5 (MAP-5+). After passaging 14% of the surviving cells were immature neurons (MAP-5+) and 4% were mature olfactory neurons (MAP-5+) and olfactory marker protein (OMP+)). In addition the same experiment was conducted on transgenic mice in which the lacZ gene was linked to the OMP promoter. Using 5-bromo-4-chloro-3-indolyl-beta-D-galactopyranoside (X-Gal) staining we showed that OMP+ cells disappeared before day 5 in culture but reappeared after passaging. These results suggest that olfactory sensory neurons can arise from a non-neuronal precursor, probably the keratin-positive horizontal **basal** cell.

11/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09870998 98288178 PMID: 9622627
Pituitary adenylate cyclase activating polypeptide (PACAP) stimulates mitogen-activated protein kinase (MAPK) in cultured rat astrocytes.
Moroo I; Tatsuno I; Uchida D; Tanaka T; Saito J; Saito Y; Hirai A
Department of Neurology, Chiba University School of Medicine, Chiba, Japan.
Brain research (NETHERLANDS) Jun 8 1998, 795 (1-2) p191-6, ISSN 0006-8993 Journal Code: 0045503
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Astrocytes, a subtype of **glial** cells, have been demonstrated to have an abundant number of receptors for pituitary adenylate cyclase activating polypeptide (PACAP), a neuropeptide of the VIP/secretin family which stimulates cAMP accumulation 1000 times more potent than VIP in astrocytes. PACAP is reported to stimulate the proliferation of astrocytes at low concentrations at which it does not yet stimulate the cAMP accumulation. In the present study, we examined the effect of PACAP on the activation of mitogen-activated protein kinase (MAPK), one of the important intracellular signals for the proliferation, and compared it with that of **epidermal** growth factor (EGF). To investigate the activation of MAPK, we focused on ERK2, one of MAPK, in cultured rat astrocytes. The activation of ERK2 was determined by immunoblotting and measurement of the activity in terms of the phosphorylating activity of immunoprecipitates with MAPK antibody on myelin basic protein. One pM of PACAP38 temporarily activated ERK2 at 10 min. In contrast, EGF activated ERK2 from 10 min to 60 min continuously. As for the dose-response effect, PACAP stimulated ERK2 at as low a concentration as 10-14 M and peaked at 10-12 M. Thereafter, its activating effect gradually decreased at 10-10 M and returned to the **basal** level at 10-8 M, forming a bell-shaped dose-dependency. Neither an inhibitor of PKA (H89) nor inhibitors of PKC (staurosporine and calphostin C) had any effect on the ERK2 activation induced by 1 pM PACAP38. Dibutyryl cAMP suppressed ERK2 activity in a dose-dependent manner. These data clearly demonstrated that PACAP stimulates MAPK in both a PKA- and a PKC-independent manner in cultured rat astrocytes.

11/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09627967 98063025 PMID: 9398461
Generation and transplantation of EGF-responsive neural stem cells derived from GFAP-hNGF transgenic mice.
Carpenter M K; Winkler C; Fricker R; Emerich D F; Wong S C; Greco C; Chen E Y; Chu Y; Kordower J H; Messing A; Bjorklund A; Hammang J P
Department of Cell and Molecular Neurobiology, CytoTherapeutics, Inc.,

Providence, Rhode Island 02906, USA.
Experimental neurology (UNITED STATES) Nov 1997, 148 (1) p187-204, ISSN 0014-4886 Journal Code: 0370712
Contract/Grant No.: NS 35708; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

EGF-responsive neural stem cells isolated from murine striatum have the capacity to differentiate into both neurons and glia in vitro. Genetic modification of these cells is hindered by a number of problems such as gene stability and transfection efficiency. To circumvent these problems we generated transgenic mice in which the human GFAP promoter directs the expression of human NGF. Neural stem cells isolated from the forebrain of these transgenic animals proliferate and form clusters, which appear identical to stem cells generated from control animals. Upon differentiation in vitro, the transgenic stem cell-derived astrocytes express and secrete bioactive hNGF. Undifferentiated GFAP-hNGF or control stem cells were transplanted into the striatum of adult rats. One and 3 weeks after transplantation, hNGF was detected immunocytochemically in an halo around the transplant sites. In GFAP-hNGF-grafted animals, intrinsic striatal neurons proximal to the graft appear to have taken up hNGF secreted by the grafted cells. Ipsilateral to implants of GFAP-hNGF-secreting cells, choline acetyltransferase-immunoreactive neurons within the striatum were hypertrophied relative to the contralateral side or control-grafted animals. Further, GFAP-hNGF-grafted rats displayed a robust sprouting of p75 neurotrophin receptor-positive fibers emanating from the underlying **basal** forebrain. These studies indicate that EGF-responsive stem cells which secrete hNGF under the direction of the GFAP promoter display in vitro and in vivo properties similar to that seen following other methods of NGF delivery and this source of cells may provide an excellent avenue for delivery of neurotrophins such as NGF to the central nervous system.

11/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09567736 97471423 PMID: 9330364
Transforming growth factor-alpha's effects on astroglial-cholinergic cell interactions in the medial septal area in vitro are mediated by alpha 2-macroglobulin.
Mazzoni I E; Kenigsberg R L
Centre de Recherche, Hopital Ste-Justine, Montreal, Quebec, Canada.
Neuroscience (UNITED STATES) Dec 1997, 81 (4) p1019-30, ISSN 0306-4522 Journal Code: 7605074
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

We reported previously that two **epidermal** growth factor receptor ligands, **epidermal** growth factor and transforming growth factor-alpha, inhibit medial septal cholinergic cell phenotypic expression (choline acetyltransferase and acetylcholinesterase activities) in vitro indirectly via (a) soluble molecule(s) released from astrocytes [Kenigsberg R. L. et al. (1992) Neuroscience 50, 85-97; Kenigsberg R. L. and Mazzoni I. E. (1995) J. Neurosci. Res. 41, 734-744; Mazzoni I. E. and Kenigsberg R. L. (1996) Brain Res. 707, 88-99]. In the present study, we found that this response to transforming growth factor-alpha is mediated, for the most part, by alpha 2-macroglobulin, a potent protease inhibitor with a wide spectrum of biological activities. In this regard, the effects of transforming growth factor-alpha on cholinergic cells can be blocked with immunoneutralizing antibodies raised against alpha 2-macroglobulin. Furthermore, western blot analysis reveals that although alpha

2-macroglobulin is present in conditioned media from control septal cultures, it is more abundant in those treated with transforming growth factor-alpha. In addition, exogenous alpha 2-macroglobulin, both in its native and trypsin-activated forms, can mimic transforming growth factor-alpha's effects on septal cholinergic cell expression. However, while the native antiprotease can slightly but significantly decrease choline acetyltransferase activity, trypsin-activated alpha 2-macroglobulin, in the nanomolar range, induces as marked a decrease in this enzyme activity as that noted with transforming growth factor-alpha. Furthermore, trypsin-activated alpha 2-macroglobulin, like **epidermal** growth factor/transforming growth factor-alpha, decreases choline acetyltransferase activity by arresting its spontaneous increase that occurs with time in culture, does so in a reversible manner and is not neurotoxic. In addition, trypsin-activated alpha 2-macroglobulin, in the nanomolar range, can affect choline acetyltransferase in a dual manner, up-regulating it at low concentrations while down-regulating it at higher ones. These responses are identical in mixed neuronal-**glial** and pure neuronal septal cultures. Furthermore, when concentrations of trypsin-activated alpha 2-macroglobulin, which alone decrease choline acetyltransferase, are added simultaneously with nerve growth factor, they serve to potentiate the nerve growth factor-induced increase in enzymatic activity. As GABAergic cell expression is not affected by alpha 2-macroglobulin, it appears that the effects of this protease inhibitor on medial septal neuronal expression are neurotransmitter-specific. Finally, trypsin-activated but not native alpha 2-macroglobulin promotes a dose-dependent aggregation of the septal neurons. This change in morphology, however, is not related to those noted in choline acetyltransferase activity. In summary, these data suggest that the expression of alpha 2-macroglobulin in astroglia from the medial septal nucleus can be controlled by **epidermal** growth factor receptor ligands to impact the functioning of **basal** forebrain cholinergic neurons.

11/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09558650 97470714 PMID: 9331174

Grafts of EGF-responsive neural stem cells derived from GFAP-hNGF transgenic mice: trophic and tropic effects in a rodent model of Huntington's disease.

Kordower J H; Chen E Y; Winkler C; Fricker R; Charles V; Messing A; Mufson E J; Wong S C; Rosenstein J M; Bjorklund A; Emerich D F; Hammang J; Carpenter M K

Research Center for Brain Repair and Department of Neurological Sciences, Rush Presbyterian Medical Center, Chicago, Illinois 60612, USA. jkordowe@rush.rpslmc.edu

Journal of comparative neurology (UNITED STATES) Oct 13 1997, 387 (1) p96-113, ISSN 0021-9967 Journal Code: 0406041

Contract/Grant No.: NS35078; NS; NINDS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The present study examined whether implants of **epidermal** growth factor (EGF)-responsive stems cells derived from transgenic mice in which the **glial** fibrillary acid protein (GFAP) promoter directs the expression of human nerve growth factor (hNGF) could prevent the degeneration of striatal neurons in a rodent model of Huntington's disease (HD). Rats received intrastriatal transplants of GFAP-hNGF stem cells or control stem cells followed 9 days later by an intrastriatal injection of quinolinic acid (QA). Nissl stains revealed large striatal lesions in rats receiving control grafts, which, on average, encompassed 12.78 mm3. The size of the lesion was significantly reduced (1.92 mm3) in rats receiving lesions and GFAP-hNGF transplants. Rats receiving QA lesions and

GFAP-hNGF-secreting grafts stem cell grafts displayed a sparing of striatal neurons immunoreactive (ir) for glutamic acid decarboxylase, choline acetyltransferase, and neurons histochemically positive for nicotinamide adenosine diphosphate. Intrastriatal GFAP-hNGF-secreting implants also induced a robust sprouting of cholinergic fibers from subjacent **basal** forebrain neurons. The lesioned striatum in control-grafted animals displayed numerous p75 neurotrophin-ir (p75NTR) astrocytes, which enveloped host vasculature. In rats receiving GFAP-hNGF-secreting stem cell grafts, the astroglial staining pattern was absent. By using a mouse-specific probe, stem cells were identified in all animals. These data indicate that cellular delivery of hNGF by genetic modification of stem cells can prevent the degeneration of vulnerable striatal neural populations, including those destined to die in a rodent model of HD, and supports the emerging concept that this technology may be a valuable therapeutic strategy for patients suffering from this disease.

11/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08908372 96254798 PMID: 8689030
Morphological differentiation of astroglial progenitor cells from EGF-responsive neurospheres in response to fetal calf serum, basic fibroblast growth factor, and retinol.
Chiang Y H; Silani V; Zhou F C
Department of Anatomy, Indiana University School of Medicine, Indianapolis 46202, USA.
Cell transplantation (UNITED STATES) Mar-Apr 1996, 5 (2) p179-89, ISSN 0963-6897 Journal Code: 9208854
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Procurement of multipotential neuroglial stem cells is possible with the addition of **epidermal** growth factor (EGF). Stem cells will differentiate into neurons and glia upon the removal of EGF from the culture medium. We have previously characterized the neuronal differentiation of stem cells derived from long-term cultured nonpassage neurospheres. In the current study, we (1) characterize the morphological differentiation of the astroglial progenitor cell from 3-mo-old neurospheres, (2) examine whether the astroglial progenitor cells from neurospheres of different brain areas exhibit different differentiation responses to the same exogenous signals, and (3) test the effects of basic fibroblast growth factor (bFGF) and retinol on differentiation. Cerebral cortex, striatum, and mesencephalon cells were obtained from Embryonic Day 14 (E-14) rat fetuses and were dissociated for the procurement of neurospheres in chemically defined medium supplemented with EGF. After 3 mo in culture, the neurospheres, derived from each of the three brain areas, were subcultured into three groups on chamber slides: (1) **basal** medium, (2) the **basal** medium plus 20 ng/mL bFGF, and (3) the **basal** medium plus 10 muM retinol. Phenotypic expression of astroglial cells was examined after 14 days subculture. Our findings indicate that the 3-mo-old cultured nonpassage neurospheres contained numerous multipotential stem cells that stained positive with nestin, and that environmental factors played an important role in influencing the differentiation of astroglial progenitor cells. As detected by **glial** fibrillary acid protein (GFAP), astroglial progenitor cells turned into protoplasmic astrocytes in the FCS-containing **basal** medium, fibrous astrocytes in the presence of bFGF, and spindle-shaped astrocytes in the presence of retinol. There were no noticeable differences in differentiation among astroglial progenitor cells of the various brain region-derived neurospheres in any of the three medium conditions. Peculiar varicosity-and growth cone-like structures on the long slender GFAP-positive processes suggest that neuroblasts and glioblast may share common morphologies,

features, or common progenitor cells during initial differentiation in vitro.

11/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08901325 96275760 PMID: 8665525
Immunohistochemical analysis of in vivo patterns of Bak expression, a proapoptotic member of the Bcl-2 protein family.
Krajewski S; Krajewska M; Reed J C
The Burnham Institute Cancer Research Center, La Jolla, California 92037, USA.
Cancer research (UNITED STATES) Jun 15 1996, 56 (12) p2849-55, ISSN 0008-5472 Journal Code: 2984705R
Contract/Grant No.: CA 60181; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The in vivo patterns of bak gene expression were determined in human tissues using an immunohistochemical approach. Polyclonal antisera were raised in rabbits against a synthetic peptide corresponding to amino acids 14-36 of the human Bak protein, and were shown to be specific by immunoblot analysis of various human tissues and cell lines. Bak immunoreactivity was detected in a wide variety of cell types and was typically present within the cytosol in a punctuate pattern suggestive of association with intracellular organelles. Consistent with a proapoptotic role for the Bak protein, gradients of Bak protein production were observed in the complex epithelia of the nasopharynx, esophagus, colon, and bladder, with Bak immunointensity being highest in the upper layers and relatively low in the **basal** portions of these epithelia. Similarly, in the myeloid series of hematopoietic cells, Bak immunoreactivity was strongest in the terminally differentiated granulocytes, with only weak immunostaining occurring in most progenitor cells in the bone marrow. Among the other cell types and tissues with prominent Bak immunostaining were: (a) cardiomyocytes; (b) vascular and visceral smooth muscle cells; (c) **basal** cells of the prostate glands; (d) myoepithelial cells of the mammary glands; (e) distal convoluted tubules of the kidney; (f) **epidermal** keratinocytes; (g) enterocytes of the small intestine; (h) Sertoli and Leidig cells of the testes; (i) theca interna cells in the ovary; and (j) adrenal cortex (but not adrenal medulla). Nearly all neurons and **glial** cells of the central nervous system did not contain immunodetectable Bak protein, whereas sympathetic neurons as well as neurons in dorsal root ganglia and their axons were Bak immunopositive. Most circulating peripheral blood lymphocytes were negative for Bak immunostaining, whereas strong Bak immunoreactivity was found frequently in lymphocytes in the nodes and spleen. Overall, these patterns of bak expression are unique compared to other members of the bcl-2 gene family, and suggest that bak regulates cell death at specific stages of cell differentiation through tissue-specific control of its expression.

11/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08605576 95365018 PMID: 7637868
Transforming growth factor-alpha immunoreactivity in the developing and adult brain.
Ferrer I; Blanco R; Carulla M; Condom M; Alcantara S; Olive M; Planas A
Unidad Neuropatologia, Hospital Principes Espana, Universidad Barcelona, Hospitalet de Llobregat, Spain.
Neuroscience (ENGLAND) May 1995, 66 (1) p189-99, ISSN 0306-4522 Journal Code: 7605074

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Transforming growth factor-alpha immunoreactivity is examined in the developing and adult brain of cats and rats, and in the adult human brain in cryostat sections immediately processed free-floating with a well-characterized monoclonal antibody which does not cross-react with **epidermal** growth factor. Transforming growth factor-alpha immunoreactivity is observed in neurons of the cerebral neocortex, subiculum, hippocampus, striatum, thalamus, amygdala, **basal** forebrain, mesencephalon, cerebellar cortex, dentate nucleus and brainstem during development and in adulthood. The intensity of the immunoreaction directly correlates with the size of the cytoplasm. Diffuse transforming growth factor-alpha immunoreactivity also occurs in the white matter of the cerebrum, cerebellum and brainstem in the kitten, but not in the adult cat. In addition to neurons, numbers of **glial** cells in the cerebellar white matter, brainstem and cerebral hemispheres during development, and a few **glial** cells in the cerebellar cortex, diencephalon, cerebral cortex and white matter in adults are strongly transforming growth factor-alpha immunoreactive. These results support the concept that transforming growth factor-alpha is widely distributed in the brain of mammals, localizes in both neurons and **glial** cells, and is development dependent. These findings also suggest that transforming growth factor-alpha may play a role in the developing and adult central nervous system.

11/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08591005 95348734 PMID: 7623068

Increased intracellular cyclic AMP levels suppress the mitogenic responses of human astrocytoma cells to growth factors.

Tsai C H; Hung L M; Cheng H P; Chen J K
Department of Neurology, Chang Gung Memorial Hospital, Taoyuan, Taiwan.

Journal of neuro-oncology (NETHERLANDS) 1995, 23 (1) p41-52, ISSN 0167-594X Journal Code: 8309335
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

It has been shown that the intracellular cAMP levels were decreased in human malignant astrocytomas. On the other hand, various growth factors and their receptors were found to be overexpressed in these tumors. It is therefore intriguing as to whether there is interplay between the two phenomena in the modulation of the astrocytoma cell growth. In a **basal** medium consisting of 75% DMEM, 25% Ham's F-12 supplemented with 2% FBS, we show that the mitogenic effects of platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), and **epidermal** growth factor (EGF) on human astrocytoma cells were suppressed by dibutyryl-cAMP. Dibutyryl-cAMP alone neither potentiated nor inhibited the tumor cell growth. Further studies show that PDGF-induced receptor autophosphorylation in human astrocytoma cells is suppressed by increased intracellular cAMP levels as measured by immunoprecipitation with anti-PDGF receptor and antiphosphotyrosine antibodies. Our results indicate that there is antagonistic interplay between the receptor tyrosine kinase pathway and cAMP-dependent protein kinase pathway in the control of the malignantly transformed **glial** cells. A reduced cAMP level seen in many human astrocytoma cells may favor their response to growth factor mitogenesis.

11/3,AB/14 (Item 14 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07895593 94030580 PMID: 8216821
Monoclonal antibody MS-44B reacts with human dendritic, **glial** and endothelial cells: differential expression of MS-44B antigen by **epidermal** dendritic cells and by MS-1+ splenic sinusoidal endothelial cells. An immunohistological study.
Goerdt S; Brocker E B; Redmann K; Ruiter D J; Gullotta F; Bergmann M; Dammrich J; Buchholz B; Dietl K H; Goters C; et al
Abteilung fur Allgemeine Dermatologie und Venerologie, Universitat Munster, BRD.
Pathobiology : journal of immunopathology, molecular and cellular biology (SWITZERLAND) 1993, 61 (1) p36-42, ISSN 1015-2008 Journal Code: 9007504
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Rat monoclonal antibody MS-44B was raised against the dendritic human melanoma cell line SK-Mel 25 and detects highly dendritic cells and endothelial cells in various human organs. Among the cells recognized are dendritic cells in lymphoid organs, such as lymph node, tonsil and spleen, dendritic cells in skin, lung and lamina propria, (astro-)**glial** cells in the central nervous system and mesangial cells in the kidney. In peripheral lymph nodes (and less consistently in visceral lymph nodes), MS-44B reactive cells are found predominantly in the paracortical area and in the region of the marginal sinus; in tonsils these dendritic cells are concentrated at the outer rim of the follicle, while their distribution in the white pulp of the spleen is less well defined. In skin, both dermal and **epidermal** dendritic cells are stained. In the dermis just beneath the dermal-**epidermal** border, dendritic cells may be found with their processes protruding into the **epidermal basal** layer. MS-44B reactive **epidermal** dendritic cells send their processes in a horizontal direction or into the upper **epidermal** cell layers. MS-44B reactive **epidermal** dendritic cells are neither Langerhans cells, since they lack HLA-DR antigens and CD1, nor Merkel cells, since they lack cytokeratin expression. They rather seem to constitute a subpopulation of **epidermal** melanocytes that are low in tyrosinase expression and do not populate the melanocyte area of the hair bulb. With regard to the endothelium, monoclonal antibody MS-44B reveals marked heterogeneity in that it preferentially stains the endothelium of large and medium-sized arterial vessels, while capillary and venous endothelia are less well stained.(ABSTRACT TRUNCATED AT 250 WORDS)

11/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07684665 93233787 PMID: 1299771
[The EGF receptor pathway in human cerebral tumors]
Etude de la voie du recepteur a l'E.G.F. dans les tumeurs cerebrales humaines.
Berger F; Laine M; Hoffmann D; Verna J M; Charffanet M; Chauvin C; Rost N ; Nissou M F; Benabid A L
Unite INSERM 318, Laboratoire de Neurobiophysique, Universite Joseph Fourier, C.H.U.R. de Grenoble.
Neuro-Chirurgie (FRANCE) 1992, 38 (5) p257-66, ISSN 0028-3770 Journal Code: 0401057
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed
The **epidermal** growth factor receptor gene is the most frequently

involved proto-oncogene in human **glial** brain tumors, in the present series in agreement with previous reports in literature. It is therefore important to study this gene from DNA to the protein product. The vicinity of cystic fluid (C.F.) to tumor cells of the cystic wall has suggested investigation of possible "E.G.F.-like" autocrine activities in C.F. In 40% of gliomas, E.G.F.-R. gene is amplified and overexpressed. This is never observed in low grade astrocytomas. In 12% of the cases, mutations of the E.G.F.-R. gene are observed. In correlation with genomic abnormalities, E.G.F.-R. is immunoprecipitated in 40% gliomas. The **basal** phosphorylation of the receptor is increased in 50% gliomas. In C.F., unexpectedly, E.G.F.-R. phosphorylation inhibitory effect is observed. Its biochemical analysis suggests an anti-tyrosine kinase activity. The observation of anti-tyrosine kinase activity in C.Fs suggests the presence of negative modulatory factors of the proto-oncogene activation in tumor tissues. This could have therapeutical interest.

11/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07649813 93164859 PMID: 8381900
CNS **glial** cells express neurotrophin receptors whose levels are regulated by NGF.
Kumar S; Pena L A; de Vellis J
Laboratory of Biomedical and Environmental Sciences, University of California, Los Angeles 90024-1759.
Brain research. Molecular brain research (NETHERLANDS) Jan 1993, 17 (1-2) p163-8, ISSN 0169-328X Journal Code: 8908640
Contract/Grant No.: HD-06576; HD; NICHD; NS-18708; NS; NINDS
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Normal CNS **glial** cells manufacture neurotrophin receptors and are competent to respond to NGF. Neurotrophins bind a common receptor (LNGFR) and ligand-specific, tyrosine kinase-containing subunits (TrkA, TrkB, or TrkC). Northern blots and transcription assays reveal complex transcriptional regulation of LNGFR in astrocytes; from undetectable **basal** levels, NGF dramatically induces LNGFR within 4-6 h. Oligodendrocytes' relatively high **basal** levels are unaffected by NGF. TrkA mRNA was undetectable, however, TrkB was present and upregulated by NGF in astrocytes but not oligodendrocytes. The results are consistent with receptor autoregulation by its ligand and suggest that NGF plays a role in normal **glial** functions.

11/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07523395 93049907 PMID: 1330655
Modulation of potassium transport in cultured retinal pigment epithelium and retinal **glial** cells by serum and **epidermal** growth factor.
Arrindell E L; McKay B S; Jaffe G J; Burke J M
Department of Ophthalmology, Medical College of Wisconsin, Milwaukee 53226.
Experimental cell research (UNITED STATES) Nov 1992, 203 (1) p192-7, ISSN 0014-4827 Journal Code: 0373226
Contract/Grant No.: EY06664; EY; NEI; P30 EY01931; EY; NEI; R01 EY04799; EY; NEI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The ionic environment of retinal photoreceptors is partially controlled

by potassium transporters on retinal **glial** and retinal pigment epithelial cells (RPE). In this study, serum and **epidermal** growth factor (EGF) were examined as modulators of potassium transport in confluent cultures of human RPE and rabbit retinal glia. EGF is a known mitogen for confluent RPE cultures and was shown here to also stimulate [3H]thymidine incorporation in cultures of retinal glia. For potassium transport studies 86Rb was used as a tracer during a 17-min incubation. For both retinal cell types the mean total 86Rb uptake in 10% serum was approximately 60% above **basal**, serum-free controls. For EGF, tested in several experiments in a concentration range from 1 to 100 ng/ml, maximal total uptake was 33 and 24% above controls for RPE and glia, respectively. Inhibitor studies suggested that **basal** and serum-stimulated uptake for both cell types occurred by the ouabain-sensitive Na-K ATPase pump and by the furosemide- or bumetanide-sensitive Na-K-Cl cotransporter. EGF-stimulated uptake appeared to be due predominantly to the cotransporter. The data suggest that serum components and EGF, which may be available to retina-derived cells under pathologic conditions, may not only stimulate proliferation but may also act as short-term modulators of potassium ion movement and thus affect physiologic processes that are sensitive to ion homeostasis.

11/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07392991 92325681 PMID: 1624933
Cholinergic differentiation in neurogenic **basal** forebrain cultures.
Martinic M; Lambert M P; Hua S; Klein W L
Department of Neurobiology and Physiology, Northwestern University, Evanston, Illinois 60208.
Journal of neurobiology (UNITED STATES) Apr 1992, 23 (3) p252-69, ISSN 0022-3034 Journal Code: 0213640
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To study early events in the central nervous system (CNS) cholinergic development, cells from rat **basal** forebrain tissue were placed in culture at an age when neurogenesis in vivo is still active [embryonic day (E) 15]. The rapid mortality of these cells in defined medium, with 50% mortality after 5-10 h, was blocked completely by soluble proteins from the olfactory bulb (a **basal** forebrain target), extending earlier observations (Lambert, Megerian, Garden, and Klein, 1988). Treated cultures were capable of incorporating thymidine into DNA, and most cells incorporating 3H-thymidine (greater than 90%) also stained positive for neurofilament, confirming neuronal proliferation in the supplemented cultures. A small percentage of 3H-thymidine labelled cells were **glial** fibrillary acidic protein (GFAP) positive, but growth factors that support astroglial proliferation [**epidermal** growth factor (EGF), basic fibroblast growth factor (bFGF), and insulin-like growth factor (IGF-1)] were not sufficient for neuronal support. After 5 culture days with supplemented medium, almost 50% of the cells showed choline acetyltransferase (ChAT) immunofluorescence. The cholinergic neurons typically formed clusters separate from noncholinergic cells. These mature cultures did not develop if young cultures were treated with aphidicolin to block DNA synthesis. The data show that cultures of very young rat **basal** forebrain cells can be neurogenic, giving rise to abundant cholinergic neurons, and that early cell proliferation is essential for long-term culture survival.

11/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07305557 92235466 PMID: 1569327
Changes of expression of intermediate filament proteins during ontogenesis of eccrine sweat glands.
Moll I; Moll R
Department of Dermatology, Mannheim Medical School, University of Heidelberg, F.R.G.
Journal of investigative dermatology (UNITED STATES) May 1992, 98 (5) p777-85, ISSN 0022-202X Journal Code: 0426720
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The intermediate filament expression in fetal and adult human eccrine sweat glands was studied by immunoperoxidase microscopy performed on cryostat sections using monoclonal antibodies against various cytokeratins (CK), vimentin, and actin. In palmar skin of 14-week-old fetuses, the early dermal cords showed a primitive CK pattern similar to that of **epidermal basal** cells. From week 15 on (distal finger skin), inner cells of the proximal (ductal) portion of the glandular anlagen expressed CK 1/10/11 and 19 (markers of adult eccrine ductal luminal cells). In addition, CK 4 was expressed in ductal luminal cells mainly in the fetal period. In the distal portion of the sweat gland anlagen the increased or new expression of the simple-epithelium-type CK 7, 8, 18, and 19 was detected at week 15, indicating the onset of the secretory differentiation pathway. Two subsegments of the prospective secretory portion could be distinguished (elongated part and end bud). Interestingly, in fetuses, most secretory portion cells co-expressed vimentin in addition to CK. From week 22 on, peripheral cells of the secretory portion were stained for CK 17 and smooth-muscle-type actin, suggesting myoepithelial differentiation. In newborn and adult eccrine glands, secretory cells expressed mainly CK 7, 8, 18, and 19, whereas myoepithelial cells were conspicuous by their co-expression of certain CK (including CK 5 and 17), vimentin, and smooth-muscle-type actin and sometimes even **glial** filament protein (GFP), similar to myoepithelial cells of other glands. These results throw further light onto the complex processes of fetal development of eccrine sweat glands and their cellular diversification. The possible biologic significance of the differential CK expression in the various glandular cell types is discussed.

11/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07240641 92185921 PMID: 1839162
EGF enhances the survival of dopamine neurons in rat embryonic mesencephalon primary cell culture.
Casper D; Mytilineou C; Blum M
Fishberg Research Center in Neurobiology, Mount Sinai School of Medicine, New York, NY 10029.
Journal of neuroscience research (UNITED STATES) Oct 1991, 30 (2) p372-81, ISSN 0360-4012 Journal Code: 7600111
Contract/Grant No.: F32 NS08600; NS; NINDS; NS-11631; NS; NINDS; NS-23017 ; NS; NINDS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Epidermal growth factor (EGF) immunoreactive material has been demonstrated to be present in the **basal** ganglia. In this study, we investigated the effect of EGF on cells cultured from 16-day embryonic rat mesencephalon, which included dopamine neurons that project to the striatum in vivo. EGF receptors were detected in untreated cultures by [125I]-EGF binding. Treatment of the cultures with EGF resulted in up to 50-fold increases in neuronal high-affinity dopamine uptake. Scatchard analysis of

uptake kinetics and counting of tyrosine hydroxylase-immunoreactive cells suggest that the effect of EGF on uptake is due to increased survival and maturation of dopaminergic neurons. By contrast, the high-affinity uptake for serotonin was increased only threefold over its controls. There was no significant effect on high-affinity gamma-aminobutyric acid (GABA) uptake. These results suggest that EGF is acting as a neurotrophic agent preferential for dopaminergic neurons in E16 mesencephalic cultures. Immunocytochemistry for **glial** fibrillary acidic protein demonstrated an increase in astroglia with EGF treatment. Fluorodeoxyuridine, an agent that is toxic to proliferating cells was able to eliminate the effect of EGF on dopamine uptake, suggesting that EGF may be increasing dopaminergic cell survival largely through a population of dividing cells.

11/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06055206 89132745 PMID: 2537015
Coincidence of EGF receptors and somatostatin receptors in meningiomas but inverse, differentiation-dependent relationship in **glial** tumors.
Reubi J C; Horisberger U; Lang W; Koper J W; Braakman R; Lamberts S W
Sandoz Research Institute, Berne, Switzerland.
American journal of pathology (UNITED STATES) Feb 1989, 134 (2) p337-44, ISSN 0002-9440 Journal Code: 0370502
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Somatostatin (SS) receptors as well as EGF receptors have been shown to be present in various brain tumors such as meningiomas or glia-derived tumors. Using receptor autoradiography for both receptors, their localization on adjacent tumor sections was investigated and a correlation was attempted. In glia-derived tumors, there was an inverse relationship for the incidence of the two receptors in individual tumors: in a majority of cases (five of eight) of well-differentiated astrocytomas (I-II), SS receptors were present, but in none of the cases (zero of eight) EGF receptors were detected. In undifferentiated glioblastomas, the reverse situation was observed, no SS receptors were found (0 of 14) but EGF receptors were present in a majority of tumors (8 of 14). In astrocytomas III both types of receptors were normally seen. These data suggest that in glia-derived tumors, SS receptors are markers for the well-differentiated cases as opposed to EGF receptors. In meningiomas, SS receptors are found in all (27 of 27) tumors and EGF receptors in a large percentage (23 of 27) of the same tumors. However, in some cases a coincidence of both receptors on the same cell can be excluded. Furthermore, no effect of the SS analog SMS 201-995 on **basal** or EGF-stimulated growth of meningiomas in culture could be detected. Nevertheless, the coexistence of the two receptor types in meningiomas may be suggestive for a potential functional interaction between EGF and SS.

11/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05899654 88331456 PMID: 3417897
The nervous system of the male Dinophilus gyrociliatus (Polychaeta, Dinophilidae): II. Electron microscopical reconstruction of nervous anatomy and effector cells.
Windoffer R; Westheide W
Spezielle Zoologie, Fachbereich Biologie/Chemie, Universitat Osnabruck, Federal Republic of Germany.
Journal of comparative neurology (UNITED STATES) Jun 22 1988, 272 (4) p475-88, ISSN 0021-9967 Journal Code: 0406041
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

All neuronal cells in the dwarf male of the dimorphic polychaete species Dinophilus gyrociliatus were individually identified by means of serial ultrathin sections. Altogether 68 neural cells--including 40 sensory neurons and 2 **glial** cells--constitute a small but complex nervous system. Fifty-three neural cells are located in three pairs of ganglia and connected by paired nerve cords. The prominent frontal ganglia, each consisting of a well-developed neuropile and surrounded by 20 or 21 neural cells, represent the animal's brain. The ventral ganglia contain only 2 neurons each. The penis ganglia--four cells each--are associated with the copulatory organ. A conspicuous circumpenial fiber mass surrounds the **basal** part of the penis. The effector cells--22 multiciliated **epidermal** cells, 34 muscle cells, and different gland cells (?)--were also reconstructed and their innervation was partly elucidated. Sensory-motor neurons were unambiguously identified. They are discussed in regard to the small body size of the animal. The male's nervous organization resembles a very simple rope ladder and may represent a reduced derivative of a nervous system in normal-sized males of monomorphic species. Similarities, however, also occur with the developing nervous system of a planktotrophic metatrochophore. The neuronal organization, with its two centers (frontal ganglia and ventral ganglia vs. penis ganglia and circumpenial fiber mass), accords well with the bipartite behavioral pattern, which is entirely devoted to locomotion and copulation, respectively.

11/3,AB/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05851380 88265829 PMID: 2455377

Intermediate filament expression in normal parotid glands and pleomorphic adenomas.

Burns B F; Dardick I; Parks W R
Department of Laboratory Medicine, Ottawa Civic Hospital, Ontario, Canada.

Virchows Archiv. A, Pathological anatomy and histopathology (GERMANY, WEST) 1988, 413 (2) p103-12, ISSN 0174-7398 Journal Code: 8302198
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

A comparative immunohistochemical study of intermediate filament expression in normal parotid glands and pleomorphic adenomas (PA) was performed using material fixed in a modified methacarn fixative. The normal myoepithelial cells of acini stained only with monoclonal antibodies 312C8-1 (cytokeratin (CK) 14) and 4.62 (CK 19) while myoepithelial/**basal** cells of ducts also reacted with antibodies 8.12 (CK 13, 16), 8.60 (CK 10, 11, +/- 1), and PKK1 (CK 7, 8, 17, 18). Normal duct luminal cells showed a different CK profile, reacting consistently with ECK, a polyclonal antibody to **epidermal** prekeratin (CK 3,6), and monoclonal antibodies 4.62, PKK1 and 8.60. In PA, tumour cells at the periphery of ducts, in solid areas, and at the edge of myxoid regions all had CK profiles similar to normal myoepithelial/**basal** cells except that antibody 4.62 was generally negative. Vimentin and **glial** fibrillary acidic protein (GFAP) were uniformly negative in normal parotids but showed variable (often strong) reactivity with some cells in chondroid, myxoid and solid areas of PA. A surprising feature of most PA was the variability of CK subtype expression not only from one case to another but also within morphologically similar areas of the same specimen. These results suggest that the morphology of PA is the result of diversity of tumour cell differentiation rather than the processes implicit in a reserve cell histogenetic model.

11/3,AB/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05850374 88257418 PMID: 3133393
Differential expression and regulation of major histocompatibility complex (MHC) products in neural and **glial** cells of the human fetal brain.
Mauerhoff T; Pujol-Borrell R; Mirakian R; Bottazzo G F
Department of Immunology, University College, London, U.K.
Journal of neuroimmunology (NETHERLANDS) Jul 1988, 18 (4) p271-89, ISSN 0165-5728 Journal Code: 8109498
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The cells of the central nervous system (CNS) have the peculiarity of physiologically expressing very low levels of HLA molecules. In multiple sclerosis (MS), however, as in endocrine autoimmune diseases, there is a marked increase of HLA expression in the tissue (i.e. the plaques) and this is attributable not only to infiltrating cells but also to the astrocytes. To gain an insight into the regulation of HLA in the different cell types in the CNS and to compare it to that observed in the endocrine organs, we have studied the effect of the lympho/monokines interferon (IFN)-alpha and -gamma, tumour necrosis factor (TNF)-alpha, and interleukin (IL)-2 and other agents on this aspect of the biology of human fetal brain cells in culture. A two-colour immunofluorescence technique which combines antibodies to diverse CNS cell markers and monoclonal antibodies (MoAbs) to the non-polymorphic region of HLA molecules was used throughout this study. In control cultures, only astrocytes expressed MHC class I, but after incubation with either IFN-gamma or TNF-alpha oligodendrocytes acquired class I expression. Surprisingly, astrocytes became spontaneously class II positive in culture and this was greatly enhanced by IFN-gamma. Other agents such as IL-2, **epidermal** growth factor, phorbolmyristate acetate and lectins had no effect. The expression of HLA molecules in the cells of the CNS both in **basal** conditions and in response to lymphokines is therefore selective and highly heterogenous, thus reflecting their intrinsic biological diversity. These findings may help to explain the features of the immunopathology of MS and also of latent viral infections of neural cells.

11/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05788128 88214947 PMID: 2452891
Effect of **epidermal** growth factor and insulin on DNA, RNA, and cytoskeletal protein labeling in primary rat astroglial cell cultures.
Avola R; Condorelli D F; Surrentino S; Turpeenoja L; Costa A; Giuffrida Stella A M
Institute of Biochemistry, Faculty of Medicine, University of Catania, Italy.
Journal of neuroscience research (UNITED STATES) Feb 1988, 19 (2) p230-8, ISSN 0360-4012 Journal Code: 7600111
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The effect of **epidermal** growth factor (EGF) and insulin on DNA, RNA, and cytoskeletal protein labeling in primary rat astroglial cell cultures was investigated. Cultures were grown for 15-30 days in vitro in 10% fetal calf serum (FCS)-supplemented medium and then maintained in serum-free **basal** medium (DMEM) supplemented with fatty acid-free

bovine serum albumin (BSA) for a starvation period of 24 hr before the addition of factors. The effect of factors was tested at different times (4, 10, 22, and 28 hr). At each time, [methyl-3H]thymidine or [5,6-3H]uridine was added to the control and treated cells; the incubation time after the addition of labeled precursors was 2 hr at 37 degrees C. The results obtained indicated that the addition of EGF or FCS significantly stimulated [methyl-3H]thymidine incorporation into DNA, reaching the maximum effect after 22 hr. EGF alone significantly stimulated [3H]uridine incorporation into RNA, and this effect was already maximum at 4 hr and remained constant up to 22 hr. The addition of insulin alone caused a slight increase in nucleic acid labeling for short times (4-10 hr). In contrast with EGF, no detectable stimulation of incorporation of labeled precursors after insulin treatment for 22 hr was observed. On the other hand, the addition of insulin in the presence of EGF induced an increase of the values observed with EGF alone on macromolecular synthesis at all the times studied. Furthermore, a decrease in cell number was observed in confluent cultures maintained for 1 week in medium containing DMEM + BSA in comparison to serum-supplemented (DMEM + BSA + FCS) cultures.

11/3,AB/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05629159 88055842 PMID: 2824252
Control of peripheral **glial** cell proliferation: a comparison of the division rates of enteric glia and Schwann cells and their response to mitogens.
Eccleston P A; Jessen K R; Mirsky R
Department of Anatomy and Developmental Biology, University College London, England.
Developmental biology (UNITED STATES) Dec 1987, 124 (2) p409-17, ISSN 0012-1606 Journal Code: 0372762
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The enteric nervous system comprises neurons and a relatively homogeneous population of **glial** cells, which differ considerably from those found in other parts of the peripheral nervous system and resemble more closely astrocytes from the central nervous system. It provides a simple model system for the study of neuron/**glial** interactions and **glial** cell development. In this study the proliferation rates of purified populations of enteric glia and Schwann cells and their response to several mitogens in vitro were compared. Enteric **glial** cells divided at a much higher rate than Schwann cells in both serum-containing and serum-free media. This difference in their **basal** proliferation rates was the major difference seen between the two cell types. Both cell populations were stimulated to divide by fibroblast growth factor and **glial** growth factor but not by **epidermal** growth factor. Enteric **glial** cells and Schwann cells proliferated at a greater rate on a basement membrane-like extracellular matrix produced by corneal endothelial cells, laminin, and fibronectin than on poly-L-lysine-coated glass coverslips. The magnitude of stimulation was greater for Schwann cells, presumably due to their lower **basal** division rates. Like Schwann cells, enteric **glial** cells were stimulated to divide by two agents which elevate intracellular cAMP, cholera toxin, and dibutyryl cAMP.

11/3,AB/27 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13923267 BIOSIS NO.: 200200552088
Lipid-mediated **glial** cell line-derived neurotrophic factor gene

transfer to cultured porcine ventral mesencephalic tissue.
AUTHOR: Bauer Matthias; Meyer Morten; Brevig Thomas; Gasser Thomas; Widmer Hans Rudolf; Zimmer Jens; Ueffing Marius(a)
AUTHOR ADDRESS: (a)Institute for Human Genetics, GSF-National Research Center for Environment and Health, Ingolstaedter Landstrasse 1, 85764, Neuherberg**Germany E-Mail: marius.ueffing@gsf.de
JOURNAL: Experimental Neurology 177 (1):p40-49 September, 2002
MEDIUM: print
ISSN: 0014-4886
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Transplantation of dopaminergic ventral mesencephalic (VM) tissue into the **basal** ganglia of patients with Parkinson's disease (PD) shows at best moderate symptomatic relief in some of the treated cases. Experimental animal studies and clinical trials with allogenic and xenogenic pig-derived VM tissue grafts to PD patients indicate that one reason for the poor outcome of neural transplantation is the low survival and differentiation of grafted dopaminergic neurons. To improve dopaminergic cell survival through a genetherapeutic approach we have established and report here results of lipid-mediated transfer of the gene for human **glial** cell line-derived neurotrophic factor (GDNF) to embryonic (E27/28) porcine VM tissue kept as organotypic explant cultures. Treatment of the developing VM with two mitogens, basic fibroblast growth factor and **epidermal** growth factor, prior to transfection significantly increased transfection yields. Expression of human GDNF via an episomal vector could be detected by in situ hybridization and by the measuring of GDNF protein secreted into the culture medium. When compared to mock-transfected controls, VM tissue expressing recombinant GDNF contained significantly higher numbers of tyrosine hydroxylase-positive neurons in the cultured VM tissue. We conclude that lipid-mediated gene transfer employed on embryonic pig VM explant cultures is a safe and effective method to improve survival of dopaminergic neurons and may become a valuable tool to improve allo- and xenotransplantation treatment in Parkinson's disease.

2002

11/3,AB/28 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13875358 BIOSIS NO.: 200200504179
Ultrastructure of the tentacle nerve plexus and putative neural pathways in sea anemones.
AUTHOR: Westfall Jane A(a); Elliott Carol F
AUTHOR ADDRESS: (a)Department of Anatomy and Physiology, Kansas State University, Manhattan, KS, 66506**USA E-Mail: westfall@vet.ksu.edu
JOURNAL: Invertebrate Biology 121 (3):p202-211 2002
MEDIUM: print
ISSN: 1077-8306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neurons of sea anemone tentacles receive stimuli via sensory cells and process and transmit information via a plexus of nerve fibers. The nerve plexus is best revealed by scanning electron microscopy of **epidermal** peels of the tentacles. The nerve plexus lies above the **epidermal** muscular layer where it appears as numerous parallel longitudinal and short interconnected nerve fibers in Calliactis parasitica. Bipolar and multipolar neurons are present and neurites form

interneuronal and neuromuscular synaptic contacts. Transmission electron microscopy of cross sections of tentacles of small animals, both C. parasitica and Aiptasia pallida, reveals bundles of 50-100 nerve fibers lying above groups of longitudinal muscle fibers separated by intrusions of mesoglea. Smaller groups of 10-50 slender nerve fibers are oriented at right angles to the circular muscle formed by the bases of the digestive cells. The unmyelinated nerve fibers lack any **glial** wrapping, although some bundles of **epidermal** fibers are partially enveloped by cytoplasmic extensions of the muscle cells; small gastrodermal nerve bundles lie between digestive epithelial cells above their **basal** myonemes. A hypothetical model for sensory input and motor output in the **epidermal** and gastrodermal nerve plexuses of sea anemones is proposed.

2002

11/3,AB/29 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13340838 BIOSIS NO.: 200100547987
Long-term proliferation and dopaminergic differentiation of human mesencephalic neural precursor cells.
AUTHOR: Storch A(a); Meissner W; Paul G; Boehm B O; Carvey P M; Kupsch A; Schwarz J
AUTHOR ADDRESS: (a)Dept. of Neurology, University of Ulm Med Sch, 89081, Ulm**Germany
JOURNAL: Society for Neuroscience Abstracts 27 (2):p1563 2001
MEDIUM: print
CONFERENCE/MEETING: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Dopamine neurons derived from neural CNS precursor cells expanded and differentiated in vitro might overcome the limited availability of appropriate tissue for restorative therapy in Parkinson's disease. Here, we report an improved method for long-term expansion and dopaminergic differentiation of human CNS precursor cells derived from the germinal region of fetal mesencephalon (6 to 9 weeks post fertilization) using serum-free media containing the mitogens EGF/FGF-2 and a reduction of atmospheric oxygen to 3%. Following incubation with striatal co-cultures from rat in differentiation media containing the cytokines IL-1b, IL-11, LIF and the growth factor GDNF, up to 1% of the precursor cells converted into cells immunoreactive for tyrosine hydroxylase (TH), a marker for dopamine neurons. These differentiated precursor cells exhibited four different DA neuron characteristics: TH and dopamine transporter, but no GABA expression, **basal** DA production and K+-evoked DA release. These precursor cells might serve as a useful source of human dopamine neurons for studying the development and degeneration of human dopamine neurons and may further serve as a continuous, on-demand source of cells for therapeutic transplantation in patients with Parkinson's disease.

2001

11/3,AB/30 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13124994 BIOSIS NO.: 200100332143

Atlas of olfactory organs of Drosophila melanogaster 2. Internal organization and cellular architecture of olfactory sensilla.
AUTHOR: Shanbhag S R; Mueller B; Steinbrecht R A(a)
AUTHOR ADDRESS: (a)Max-Planck-Institut fuer Verhaltensphysiologie, 82319, Seewiesen: steinbrecht@mpi-seewiesen.mpg.de**Germany
JOURNAL: Arthropod Structure & Development 29 (3):p211-229 2000
MEDIUM: print
ISSN: 1467-8039
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Antennae and maxillary palps of Drosophila melanogaster were studied with the electron microscope on serial sections of cryofixed specimens. The number of **epidermal** cells roughly equals the number of sensilla, except for regions where the latter are scarce or absent. Each **epidermal** cell forms about two non-innervated spinules, a prominent subcuticular space and a conspicuous **basal** labyrinth, suggesting a high rate of fluid transport through the sensory epithelium. The internal organization and fine structure of trichoid, intermediate and basiconic sensilla is very similar. Receptor cell somata are invested by thin **glial** sheaths extending distad to the inner dendritic segments. Further distally, the thecogen cell forms a sleeve around the dendrites, but an extracellular dendrite sheath is absent. At the base of the cuticular apparatus, the inner sensillum-lymph space around the ciliary and outer dendritic segments is confluent with the large outer sensillum-lymph space formed by the trichogen and tormogen cells. All three auxiliary cells exhibit many features of secretory and transport cells but extend only thin **basal** processes towards the haemolymph sinus. The bauplan and fine structure of coeloconic sensilla differs in the following aspects: (1) the ciliary segment of the dendrites is located deeper below the base of the cuticular apparatus than in the other sensillum types; (2) a prominent dendrite sheath is always present, separating inner and outer sensillum-lymph spaces completely; (3) the apical microlamellae of the auxiliary cells are more elaborate, but free sensillum-lymph spaces are almost absent; (4) there are always four not three auxiliary cells. Morphometric data are presented on the diameter of inner and outer dendritic segments and on the size of receptor cells, as well as of the receptor and auxiliary cell nuclei. The special fine structural features of Drosophila olfactory sensilla are discussed under the aspects of sensillar function and the localization of proteins relevant for stimulus transduction.

2000

11120006 BIOSIS NO.: 199799741151
The cellular structure for the afferent link of the skin nervous plexus of phoronids (Tentaculata, Phoronoidea) metasome.
AUTHOR: Lagutenko Yu P
AUTHOR ADDRESS: I.P. Pavlov Inst. Physiol., Russ. Acad. Sci., St. Petersburg**Russia
JOURNAL: Zhurnal Evolyutsionnoi Biokhimii i Fiziologii 32 (4):p448-459 1996
ISSN: 0044-4529
RECORD TYPE: Abstract
LANGUAGE: Russian; Non-English
SUMMARY LANGUAGE: Russian; English

ABSTRACT: The basiepidermal nervous plexus of Phoronopsis harmeri metasome has been stained in the living animals with methylene blue. 24 varieties of the sensory neurons were detected. The sensory neuropile in Ph. harmeri demonstrates the significant structural peculiarity based on location not only in the **basal** layer of epidermis but in the supportive and **glial epidermal** cells. The bilateral symmetry for somae and fibers of the sensory neurons was not revealed. It shows that sensory neuropile Phoronids distinguishes from latter of Articulata and similar to the primitive turbellarians, Enteropneusta and echinoderms. It was determined that a part of the sensory cells dendrites does not reach the surface of the animal body. There are bi- and multipolar cells and transitional forms among sensory neurons. It was assumed that sensory neuropile of the studied phoronids demonstrates a very primitive state of the afferent link in this group of animals.

1996

11/3,AB/32 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10325044 BIOSIS NO.: 199698779962
Plasticity of astrocytes derived from aged mouse cerebral hemispheres: Changes with cell passage and immortalization.
AUTHOR: Grove Jerome; Gomez Julissa; Kentroti Susan; Vernadakis Antonia(a)
AUTHOR ADDRESS: (a)Dep. Pharmacol., Univ. Colo. Health Sci. Cent., 4200 E. 9th Ave., Denver, CO 80206**USA
JOURNAL: Brain Research Bulletin 39 (4):p211-217 1996
ISSN: 0361-9230
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: This study was targeted at the beginning to understand the functional status of **glial** cells derived from aged brain. We have previously characterized passaged cell cultures derived from aged mouse cerebral hemispheres (MACH) and found them to contain large populations of astrocytes, type 1, as well as limited numbers of astrocytes, type 2, oligodendrocytes, and progenitor cells. Using the activity of the astrocyte marker, glutamine synthetase (GS), as an index, we found that MACH astrocytes continue to respond to several microenvironmental signals, including the cAMP-enhancing agents dibutyryl cAMP and R020-1724 (an inhibitor of phosphodiesterase). In addition, whereas the **basal** activity of GS increased with cell passage, their response to these agents was cell-passage dependent, increasing at early (21-22) passages and decreasing at later (4651) passages. Because neurotrophins (i.e., NGF and EGF) also provide microenvironmental signals essential to normal **glial** function, MACH cultures were assessed for their response to these factors. MACH cultures at passage 35 responded to treatment with NGF and EGF with a dose-dependent increase in GS activity by both neurotrophins. With the intention of arresting these cultures at a specific stage of differentiation, these cells were immortalized at passage 19 by transfection with the gene encoding SV40 Large T antigen. These immortalized MACH responded to exposure to dBcAMP and R020-1724 with a marked decrease in GS activity, mimicking the response of normal MACH glia at late passage. Finally, because it has been shown that glia from both immature and adult brain contain neurotrophins and respond to neurotrophins via a receptor-mediated pathway, we examined expression of NGF protein as well as NGF (p-75) and EGF receptor protein in various passages and colonies of normal and immortalized MACH cultures. We found a consistent expression of all three proteins in the various cell populations. Results of this study suggest that astrocytes from aging brain continue to function normally with respect to several parameters

(i.e., response to neurotrophins and differentiating agents). Thus, they retain their plasticity to a great degree through early cell passages. However, with advancing cell passage this plasticity declines and cell homeostasis is impaired. We propose, therefore, that astrocytes undergo several critical periods in their functional lifespan, one of which is represented by the functional transition demonstrated in this study.

1996

11/3,AB/33 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10026248 BIOSIS NO.: 199598481166
Compartmental expression patterns of the CD15 epitope and of the **epidermal** growth factor receptor (EGFr) within the human ganglionic eminence.
AUTHOR: Mai J K; Lensing-Hoehn S
AUTHOR ADDRESS: Dep. Neuroanatomy, H.-Heine-Univ., Moorenstr. 5, D-40001 Duesseldorf**Germany
JOURNAL: Society for Neuroscience Abstracts 21 (1-3):p792 1995
CONFERENCE/MEETING: 25th Annual Meeting of the Society for Neuroscience San Diego, California, USA November 11-16, 1995
ISSN: 0190-5295
RECORD TYPE: Citation
LANGUAGE: English
1995

11/3,AB/34 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09922430 BIOSIS NO.: 199598377348
Morphogenesis of the antenna of the male silkmoth, Antheraea polyphemus. V. Development of the peripheral nervous system.
AUTHOR: Steiner Cornelia; Keil Thomas A
AUTHOR ADDRESS: Max-Planck-Inst. Verhaltensphysiologie, Arbeitsgruppe Kaissling D-82319 Seewiesen**Germany
JOURNAL: Tissue & Cell 27 (3):p275-288 1995
ISSN: 0040-8166
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The imaginal antenna of the male silkmoth Antheraea polyphemus is a feather-shaped structure consisting of about 30 flagellomeres, each of which gives off two pairs of side branches. During the pupal stage (lasting for 3 weeks), the antenna develops from a leaf-shaped, flattened **epidermal** sac ('antennal blade') via two series of incisions which proceed from the periphery towards the prospective antennal stem. The development of the peripheral nervous system was studied by staining the neurons with an antibody against horseradish peroxidase as well as by electron microscopy. The epithelium is subdivided in segmentally arranged sensillogenic regions alternating with non-sensillogenic regions. Immediately after apolysis, clusters consisting of 5 sensory neurons each and belonging to the prospective sensilla chaetica can be localized at the periphery of the antennal blade in the sensillogenic regions. During the first day following apolysis, the primordia of ca. 70000 olfactory sensilla arise in the sensillogenic regions. Axons from their neurons are collected in segmentally arranged nerves which run towards the CNS along the dorsal as well as the ventral epidermis and are enveloped by a **glial** sheath. This 'primary innervation pattern' is completed

within the second day after apolysis. A first wave of incisions ('primary incisions') subdivide the antennal blade into segmental 'double branches' without disturbing the innervation pattern. Then a second wave of incisions ('secondary incisions') splits the double branches into single antennal branches. During this process, the segmental nerves and their **glial** sheaths are disintegrated. The axons are then redistributed into single branch nerves while their **glial** sheath is reconstituted, forming the 'secondary', or adult, innervation pattern. The epidermis is backed by a **basal** lamina which is degraded after outgrowth of the axons, but is reconstituted after formation of the single antennal branches.

1995

11/3,AB/35 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08762564 BIOSIS NO.: 199395051915
EGF receptor pathway in human brain tumors.
AUTHOR: Berger F; Laine M; Hoffmann D; Verna J M; Charffanet M; Chauvin C; Rost N; Nissou M-F; Benabid A-L(a)
AUTHOR ADDRESS: (a)Unite INSERM 318, Lab. de Neurobiophysique, Universite Joseph Fourier, C.H.R.U. de Grenoble, B.P**anada
JOURNAL: Neuro-chirurgie 38 (5):p257-266 1992
ISSN: 0028-3770
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English; French

ABSTRACT: The **epidermal** growth factor receptor gene is the most frequently involved proto-oncogene in human **glial** brain tumors, in the present series in agreement with previous reports in literature. It is therefore important to study this gene from DNA to the protein product. The vicinity of cystic fluid (C.F.) to tumor cells of the cystic wall has suggested investigation of possible "E.G.F.-like" autocrine activities in C.F. In 40% of gliomas, E.G.F.-R. gene is amplified and overexpressed. This is never observed in low grade astrocytomas. In 12% of the cases, mutations of the E.G.F.-R. gene are observed. In correlation with genomic abnormalities, E.G.F.-R. is immunoprecipitated in 40% gliomas. The **basal** phosphorylation of the receptor is increased in 50% gliomas. In C.F., unexpectedly, E.G.F.-R. phosphorylation inhibitory effect is observed. Its biochemical analysis suggests an antityrosine kinase activity. The observation of antityrosine kinase activity in C.Fs suggests the presence of negative modulatory factors of the proto-oncogene activation in tumor tissues. This could have therapeutical interest.

1992

11/3,AB/36 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07331921 BIOSIS NO.: 000090111823
EYE STRUCTURE OF OPHRYOTROCHA-PUERILIS POLYCHAETA DORVILLEIDAE
AUTHOR: RHODE B
AUTHOR ADDRESS: INSTITUT FUER ZOOLOGIE DER FREIEN UNIVERSITAET BERLIN, 1000 BERLIN 33, WEST GERMANY.
JOURNAL: J MORPHOL 205 (2). 1990. 147-154. 1990
FULL JOURNAL NAME: Journal of Morphology

CODEN: JOMOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The protandric hermaphrodite Ophryotrocha puerilis possesses one pair of eyes. They are located in the peristomium. Each light-sensitive organ consists of one sensory cell and one to two supporting cell(s) embedded in a cup-shaped reflector. The sensory-supporting cell complex is enveloped by a **basal** lamina. This lamina is supposed to be identical with the neural lamella. Thus, the eyes proper have to be regarded as protrusions from the brain, while **epidermal** cells seem to differentiate to crystalline cells (reflector) and are deposited onto the sensory complex. The reflector is built up by several cup-shaped cells (juveniles, 4-5, adults, 10-12). Each of these cells comprises a multilayer of parallel-oriented, membrane-bound crystalline platelets which are thought to be guanine. The sensory cell is of the inverted rhabdomere type. Submicrovillar cisternae, typical for most polychaete eyes, are lacking. The first and always present supporting cell entirely envelops the sensory cell, thus forming the extracellular space around the rhabdomere. It does not contain any pigment granules. Often but always a second supporting cell has been observed surrounding the sensory cell and first support cell. It is interpreted as a **glial** cell. In the sensory cell beneath the rhabdomere, pino- and phagocytosis can be observed and secondary lysosomes are found in high densities. Preliminary results seem to demonstrate that there is no distinct diurnal cycle of receptoral membrane recycling. In comparison with the ocelli of Dinophilidae, which have been interpreted as a dorvilleid-related family, morphological differences and their application to phylogenetic considerations are discussed.

1990

11/3,AB/37 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03282066 BIOSIS NO.: 000072010169
FINE STRUCTURE OF THE BODY WALL NERVOUS SYSTEM AND DIGESTIVE TRACT IN THE LOBATOCEREBRIDAE AND ORGANIZATION OF THE GLIO INTERSTITIAL SYSTEM IN ANNELIDA
AUTHOR: RIEGER R M
AUTHOR ADDRESS: DEP. ZOOL., UNIV. N.C., CHAPEL HILL, N.C. 27514.
JOURNAL: J MORPHOL 167 (2). 1981. 139-166. 1981
FULL JOURNAL NAME: Journal of Morphology
CODEN: JOMOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The family Lobatocerebridae, Rieger, contains a group of turbellariomorph worms [including Lobatocerebrum psammicola Rieger and Lobatocerebrum sp.1] in the annelid line of evolution. The fine structural organization of the body wall, the digestive tract and parts of the central and peripheral nervous sytem are described and the findings are discussed in light of general invertebrate cytology. The epidermis and gastrodermis contain a **basal** granule cell system which is structurally very similar to the neuroglia cell system of the nervous system. The continuity of the neuroglia cell system, the **epidermal basal** granule cell system and the **basal** granule cell system in the digestive epithelia suggests the existence of a single **glial-basal** granule cell system, similar to the gliointerstitial cell system 1st recognized in the Mollusca. The Annelida may show a dual (ectodermal and mesodermal) origin of such a gliointerstitial cell system as suggested by similarities in the

epidermal basal cell system in the Oligochaeta and of certain **epidermal** and gastrodermal cells in polychaete regeneration with neuroglia in the Annelida. The structural similarity of neuroglia and **basal** granule cells in Lobatocerebridae may be the result of similarity in the formation, maintenance or regulation of the extracellular matrix.

1981

11/3,AB/38 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

01965141 BIOSIS NO.: 000062055253
ORIGIN AND MORPHOGENESIS OF SENSORY NEURONS IN AN INSECT ANTENNA
AUTHOR: SANES J R; HILDEBRAND J G
JOURNAL: DEV BIOL 51 (2). 1976 300-319. 1976
FULL JOURNAL NAME: Developmental Biology
CODEN: DEBIA
RECORD TYPE: Abstract

ABSTRACT: Each antennal flagellum of the moth, Manduca sexta contains .apprx. 2.5 .times. 105 primary sensory neurons. The neurons are components of small sensory organs (sensilla) and send axons through antennal nerves to the brain. The neurons, sensilla and nerves differentiate as the antenna develops, during the 18 days of metamorphosis from pupa to adult. Neurons arise from divisions of **epidermal** cells between 25-60 h after pupal ecdysis and elaborate axons and dendrites soon thereafter. Neurons have the bipolar form, ciliated dendrite and **glial** sheath characteristic of the adult within a few days of their birth. The axons grow along small pupal nerves to form the adult antennal nerves, and the dendrites grow beyond the apical margin of the epidermis where they are enveloped by a growing process of the sensilla's trichogen cell. Cuticle secreted by the trichogen cell forms the seta or sensory hair of the sensillum. Later the neuronal somata migrate from the **basal** to the apical margin of the epidermis. Finally, the cytoplasm withdraws from the seta, leaving the dendrites imprisoned in a cylinder of cuticle. All the neurons in the flagellum differentiate nearly synchronously, facilitating correlation of morphogenetic results with biochemical and electrophysiological analyses of the developing neurons.

1976

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epidermal and basal and cell
          117035  EPIDERMAL
          301830  BASAL
         3764905  CELL
     S12    6602  EPIDERMAL AND BASAL AND CELL
? s s12 and culture and (transform or transfect)
            6602  S12
          692228  CULTURE
           32767  TRANSFORM
            1502  TRANSFECT
     S13      10  S12 AND CULTURE AND (TRANSFORM OR TRANSFECT)
? rd
...completed examining records
     S14       8  RD (unique items)
? t s14/3,ab/all

 14/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11202009   21221186   PMID: 11320407
  Direct transfection and activation of human cutaneous dendritic cells.
  Larregina A T; Watkins S C; Erdos G; Spencer L A; Storkus W J; Beer Stolz
D; Falo L D
  Department of Dermatology, University of Pittsburgh, School of Medicine,
Pittsburgh, PA, USA.
  Gene therapy (England)  Apr 2001,  8  (8)  p608-17,  ISSN 0969-7128
Journal Code: 9421525
  Contract/Grant No.: PO1 AI 43664; AI; NIAID; R21AI 469701; AI; NIAID
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Gene therapy techniques can be important tools for the induction and
control of immune responses. Antigen delivery is a critical challenge in
vaccine design, and DNA-based immunization offers an attractive method to
deliver encoded transgenic protein antigens. In the present study, we used
a gene gun to transfect human skin organ cultures with a particular
goal of expressing transgenic antigens in resident cutaneous dendritic
cells. Our studies demonstrate that when delivered to human skin, gold
particles are observed primarily in the epidermis, even when high helium
delivery pressures are used. We demonstrate that Langerhans cells resident
in the basal epidermis can be transfected, and that biolistic gene
delivery is sufficient to stimulate the activation and migration of skin
dendritic cells. RT-PCR analysis of dendritic cells, which have migrated
from transfected skin, demonstrates the presence of transgenic mRNA,
indicating direct transfection of cutaneous dendritic cells. Importantly,
transfected epidermal Langerhans cells can efficiently present a
peptide derived from the transgenic melanoma antigen MART-1 to a
MART-1-specific CTL. Taken together, our results demonstrate direct
transfection, activation, and antigen-specific stimulatory function of in
situ transduced human Langerhans cells.


 14/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10317411   99292884   PMID: 10364340
  The human papillomavirus type 16 E6 gene alone is sufficient to induce
carcinomas in transgenic animals.
  Song S; Pitot H C; Lambert P F
  McArdle Laboratory for Cancer Research, University of Wisconsin Medical
School, Madison, Wisconsin 53706, USA.
  Journal of virology (UNITED STATES)  Jul 1999,  73  (7)  p5887-93,
ISSN 0022-538X  Journal Code: 0113724
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Contract/Grant No.: CA07175; CA; NCI; CA22443; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

High-risk human papillomaviruses (HPVs) are the causative agents of certain human cancers. HPV type 16 (HPV16) is the papillomavirus most frequently associated with cervical cancer in women. The E6 and E7 genes of HPV are expressed in cells derived from these cancers and can **transform** cells in tissue **culture** . Animal experiments have demonstrated that E6 and E7 together cause tumors. We showed previously that E6 and E7 together or E7 alone could induce skin tumors in mice when these genes were expressed in the **basal** epithelia of the skin. In this study, we investigated the role that the E6 gene plays in carcinogenesis. We generated K14E6 transgenic mice, in which the HPV16 E6 gene was directed in its expression by the human keratin 14 promoter (hK14) to the **basal** layer of the epidermis. We found that E6 induced cellular hyperproliferation and **epidermal** hyperplasia and caused skin tumors in adult mice. Interestingly, the tumors derived from E6 were mostly malignant, as opposed to the tumors from E7 mice, which were mostly benign. This result leads us to hypothesize that E6 may contribute differently than E7 to HPV-associated carcinogenesis; whereas E7 primarily contributes to the early stages of carcinogenesis that lead to the formation of benign tumors, E6 primarily contributes to the late stages of carcinogenesis that lead to malignancy.

14/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09065446 96434806 PMID: 8837730

Inhibition by tunicamycin of mucin synthesis, not morphological changes, in epidermis during retinol-induced mucous metaplasia of chick embryonic cultured skin.

Obinata A; Akimoto Y; Kawamata T; Shimizu S; Hirano H
Department of Physiological Chemistry, Faculty of Pharmaceutical Sciences, Teikyo University, Kanagawa, Japan.

Anatomical record (UNITED STATES) Aug 1996, 245 (4) p715-23, ISSN 0003-276X Journal Code: 0370540
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

BACKGROUND: Our previous studies have shown that **epidermal** mucous metaplasia of chick embryonic skin can be induced by **culture** in medium containing 20 microM retinol for only 8 hr and then in a chemically defined medium without retinol for 2 days and that retinol primarily affects the dermal cells, which then **transform** the epithelial cells into mucus-secreting cells. METHODS: Tarsometatarsal skin of 13-day-old chick embryo was cultured with 20 microM retinol for 1 day and then without the vitamin but with 0.1 microgram/ml tunicamycin for 5 days. Effect of tunicamycin on **epidermal** mucous metaplasia was studied biochemically and morphologically. RESULTS: Tunicamycin, which prevents the formation of N-glycans and inhibits maturation or morphological organization of various epithelial cells, irreversibly inhibited the synthesis of sulfated glycoproteins (O-glycans, mucin) in the epidermis only when applied to retinol-pretreated skin. Microvilli on the surface of the cells were well developed, but mucous granules surrounded by a limiting membrane were not observed in the upper **cell** layer of the epidermis, and many vesicles without electron-dense materials (mucin) and dilated rough endoplasmic reticulum were seen in the intermediate **cell** layers of the epidermis. When recombinants of 13-day-old normal epidermis and cultured dermis, which had been treated with retinol for 24 hr and with only tunicamycin for 2 days, were cultured without the antibiotic for 5 days, **epidermal**

mucous metaplasia was induced. CONCLUSION: These results suggest that tunicamycin did not prevent morphological changes induced by retinol but inhibited mucin synthesis by a direct action on the epidermis of retinol-pretreated skin. Because in some **cell**-line mucin precursors contain high mannose N-linked oligosaccharides side chains, tunicamycin may have inhibited mucin synthesis. Interaction between **epidermal** **basal** cells and retinol-pretreated dermal fibroblasts is prerequisite for **epidermal** mucous metaplasia. Thus, the present study suggests that N-linked protein glycosylation is not required for this interaction.

14/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07400229 92334861 PMID: 1630815
The HIV tat gene transforms human keratinocytes.
Kim C M; Vogel J; Jay G; Rhim J S
Laboratory of Virology, Jerome H. Holland Laboratory, Rockville, Maryland 20855.
Oncogene (ENGLAND) Aug 1992, 7 (8) p1525-9, ISSN 0950-9232 Journal Code: 8711562
Contract/Grant No.: CA53633; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Skin disorders are frequently seen in patients with the acquired immune deficiency syndrome (AIDS). Since many of these cutaneous manifestations are accompanied by an early onset of **epidermal** hyperplasia, the keratinocyte is a candidate for infection by the human immunodeficiency virus (HIV). We now report that the HIV tat gene, under the control of the viral long terminal repeat (LTR), can efficiently **transform** human keratinocytes in **culture**. Our finding suggests that this activity of the tat gene may be responsible for the **epidermal** hyperplasia that accompanies psoriasis and precedes the development of squamous **cell** and **basal cell** carcinomas in AIDS patients.

14/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06946626 91256378 PMID: 2044193
A comparison of interfollicular and hair follicle derived cells as targets for the v-rasHa oncogene in mouse skin carcinogenesis.
Weinberg W C; Morgan D L; George C; Yuspa S H
Laboratory of Cellular Carcinogenesis and Tumor Promotion, National Cancer Institute, Bethesda, MD 20892.
Carcinogenesis (UNITED STATES) Jun 1991, 12 (6) p1119-24, ISSN 0143-3334 Journal Code: 8008055
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Methods to isolate and **culture** intact mouse hair follicles and interfollicular **epidermal** cells provide a model to test the potential of each to form tumors as a consequence of rasHa gene activation and to determine the risk for progression in the resultant tumors. The v-rasHa oncogene was introduced into intact or dissociated hair follicle cells or interfollicular **epidermal** cells from newborn mouse skin via a defective retroviral vector. Either immediately after infection or after an additional 6 days of **culture**, the v-rasHa cells were transferred to nude mice as a skin graft. Both **cell** populations formed squamous papillomas which were indistinguishable based on morphology and immunocytochemistry. All papillomas expressed **epidermal** specific

markers whether derived from hair follicle or interfollicular cells, and many regressed. After 16 weeks in vivo, 20-30% of the benign skin tumors in all groups converted to malignancy. In addition to papillomas, hair follicle derived populations produced hemangiomas in many animals. None of the groups formed **basal cell** carcinomas, keratoacanthomas or tumors with characteristics of differentiating hair follicle cells. These studies indicate that ras gene activation can contribute to benign squamous neoplasia originating from several skin-derived **cell** types. The underlying factors which determine the variable risk for neoplastic progression of skin papillomas after ras gene activation is not simply the origin of the tumor **cell** from hair follicle or interfollicular epidermis. The activated ras oncogene can also **transform** skin endothelial cells but does not appear to directly contribute to transformation of the more differentiated cells of the hair follicle.

14/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06148113 89235283 PMID: 2654301
Use of human **epidermal** cells in the study of carcinogenesis.
Kuroki T; Chida K; Hosomi J; Kondo S
Department of Cancer Cell Research, Institute of Medical Science, Tokyo, Japan.
Journal of investigative dermatology (UNITED STATES) May 1989, 92 (5 Suppl) p271S-274S, ISSN 0022-202X Journal Code: 0426720
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Because of the importance of human cells, particularly human epithelial cells, in cancer research, we have studied certain phases or events of carcinogenesis using human **epidermal** cells in primary **culture**. 1) We found that human **epidermal** cells are capable of metabolizing benzo[a]pyrene. Large inter-individual variations are found in the **basal** and induced arylhydrocarbon-hydroxylase activities. 2) UV-induced unscheduled DNA synthesis was demonstrated in human **epidermal** cells on autoradiographs. We also found that DNA repair is defective in **epidermal** cells isolated from xeroderma pigmentosum by a new explant-outgrowth **culture**. 3) Human **epidermal** cells are unique in that there is a large number of binding sites to phorbol esters compared with mouse **epidermal** cells, but there is no down-regulation. Further, human **epidermal** cells show essentially negative responses to tumor promoters, i.e., no stimulation of DNA synthesis, sugar uptake, and no induction of ornithine decarboxylase activity. 4) Human **epidermal** cells contain 1.5 x 10(5) binding sites per **cell** for **epidermal** growth factor (EGF), whereas squamous **cell** carcinomas of skin and oral cavity have larger amounts of EGF receptors in the order of 10(6) per **cell**. 5) Based on the above results, we attempted to **transform** human **epidermal** cells by the treatment with chemical carcinogens, but until now no transformation was obtained.

14/3,AB/7 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09681084 BIOSIS NO.: 199598136002
Induction of mucous metaplasia in chick embryonic skin by retinol-pretreated embryonic chick or quail dermal fibroblasts through **cell-cell** interaction: Correlation of a transient increase in retinoic acid receptor beta mRNA in retinol-treated dermal fibroblasts with their competence to induce **epidermal** mucous metaplasia.
AUTHOR: Obinata Akiko(a); Akimoto Yoshihiro; Kawamata Takashi(a); Hirano

Hiroshi
AUTHOR ADDRESS: (a)Dep. Physiol. Chem., Fac. Pharm. Sci., Teikyo Univ., Sagamiko, Kanagawa 199-01**Japan
JOURNAL: Development Growth & Differentiation 36 (6):p579-587 1994
ISSN: 0012-1592
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: **Epidermal** mucous metaplasia of 13-day-old chick embryonic tarsometatarsal skin can be induced by **culture** in medium containing 20 mu-M retinol for only 8 hr and then in a chemically defined medium without retinol for 2 days. Retinol primarily affects the dermal cells, which then **transform** the epithelial cells into mucus-secreting cells. In this study, we developed a system using a combination of retinol-pretreated chick or quail dermal fibroblasts and chick skin, and showed that retinol-pretreated quail embryonic dermal fibroblasts invaded the dermis of chick embryonic skin to beneath the **epidermal basal** cells within 1 day of **culture** and induced metaplasia, suggesting that **epidermal** mucous metaplasia of the skin was induced by the direct interaction of retinol-pretreated dermal fibroblasts with the **epidermal** cells or by low diffusible paracrine factor produced by the fibroblasts. Increase in retinoic acid receptor beta (RAR-beta) mRNA in dermal fibroblasts was observed after 8 hr-treatment with retinol which preceded morphological changes induced by retinol and this increase was correlated with the competence of the dermal fibroblasts to induce **epidermal** mucous metaplasia. Thus some gene product(s) controlled by RAR-beta in dermal fibroblasts may be an essential signal for induction of **epidermal** mucous metaplasia.

1994

14/3,AB/8 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07730026 BIOSIS NO.: 000092054657
A COMPARISON OF INTERFOLLICULAR AND HAIR FOLLICLE DERIVED CELLS AS TARGETS FOR THE V-RAS-H-A ONCOGENE IN MOUSE SKIN CARCINOGENESIS
AUTHOR: WEINBERG W C; MORGAN D L; GEORGE C; YUSPA S H
AUTHOR ADDRESS: LAB. CELLULAR CARCINOGENESIS TUMOR PROMOTION, DIV. CANCER ETIOL., NATIONAL CANCER INST., BETHESDA, MD. 20892.
JOURNAL: CARCINOGENESIS (EYNSHAM) 12 (6). 1991. 1119-1124. 1991
CODEN: CRNGD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Methods to isolate and **culture** intact mouse hair follicles and interfollicular **epidermal** cells provide a model to test the potential of each to form tumors as a consequence of rasHa gene activation and to determine the risk for progression in the resultant tumors. The v-rasHa oncogene was introduced into intact or dissociated hair follicle cells or interfollicular **epidermal** cells from newborn mouse skin via a defective retroviral vector. Either immediately after infection or after an additional 6 days of **culture**, the v-rasHa cells were transferred to nude mice as a skin graft. Both **cell** populations formed squamous papillomas which were indistinguishable based on morphology and immunohistocytochemistry. All papillomas expressed **epidermal** specific markers whether derived from hair follicle or interfollicular cells, and many regressed. After 16 weeks in vivo, 20-30% of the benign skin tumors in all groups converted to malignancy. In addition to papillomas, hair follicle derived populations produced hemangiomas in many animals. None of the groups formed **basal**

cell carcinomas, keratoacanthomas or tumors with characteristics of differentiating hair follicle cells. These studies indicate that ras gene activation can contribute to benign squamous neoplasia originating from several skin-derived **cell** types. The underlying factors which determine the variable risk for neoplastic progression of skin papillomas after ras gene activation is not simply the origin of the tumor **cell** from hair follicle or interfollicular epidermis. The activated ras oncogene can also **transform** skin endothelial cells but does not appear to directly contribute to transformation of the more differentiated cells of the hair follicle.

1991

```
 s neurod1 or neurod2
              84  NEUROD1
              49  NEUROD2
     S15     123  NEUROD1 OR NEUROD2
? s s15 and transcription
             123  S15
          362053  TRANSCRIPTION
     S16      99  S15 AND TRANSCRIPTION
? s s16 and basal
              99  S16
          301830  BASAL
     S17       2  S16 AND BASAL
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? t s18/3,ab/all

 18/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10575349   20094969   PMID: 10629047
  The homeodomain of PDX-1 mediates multiple protein-protein interactions
in the formation of a transcriptional activation complex on the insulin
promoter.
  Ohneda K; Mirmira R G; Wang J; Johnson J D; German M S
  Hormone Research Institute, University of California, San Francisco, San
Francisco, California, USA.
  Molecular and cellular biology (UNITED STATES) Feb 2000, 20 (3)
 p900-11, ISSN 0270-7306 Journal Code: 8109087
  Contract/Grant No.: DK-21344; DK; NIDDK
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Activation of insulin gene transcription specifically in the
pancreatic beta cells depends on multiple nuclear proteins that interact
with each other and with sequences on the insulin gene promoter to build a
transcriptional activation complex. The homeodomain protein PDX-1
exemplifies such interactions by binding to the A3/4 region of the rat
insulin I promoter and activating insulin gene transcription by
cooperating with the basic-helix-loop-helix (bHLH) protein E47/Pan1, which
binds to the adjacent E2 site. The present study provides evidence that the
homeodomain of PDX-1 acts as a protein-protein interaction domain to
recruit multiple proteins, including E47/Pan1, BETA2/NeuroD1, and
high-mobility group protein I(Y), to an activation complex on the E2A3/4
minienhancer. The transcriptional activity of this complex results from the
clustering of multiple activation domains capable of interacting with
coactivators and the basal transcriptional machinery. These
interactions are not common to all homeodomain proteins: the LIM
homeodomain protein Lmx1.1 can also activate the E2A3/4 minienhancer in
cooperation with E47/Pan1 but does so through different interactions.
Cooperation between Lmx1.1 and E47/Pan1 results not only in the aggregation
of multiple activation domains but also in the unmasking of a potent
activation domain on E47/Pan1 that is normally silent in non-beta cells.
While more than one activation complex may be capable of activating insulin
gene transcription through the E2A3/4 minienhancer, each is dependent
on multiple specific interactions among a unique set of nuclear proteins.
? ds

Set     Items   Description
S1      60600   GLIAL
S2       7186   S1 AND CULTURE
S3         19   S2 AND TRANSFORM
S4         13   RD (unique items)
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S5        1250   S1 AND REVIEW
S6           0   S5 AND (NEUROD1 OR NEUROD2 OR ASH1 OR ZIC1 OR ZIC2 OR ZIC3
                 OR MYT1)
S7           0   S5 AND MSX
S8           0   S5 AND HES
S9           0   S5 AND EPIDERMAL AND BASAL
S10         59   S1 AND EPIDERMAL AND BASAL
S11         38   RD (unique items)
S12       6602   EPIDERMAL AND BASAL AND CELL
S13         10   S12 AND CULTURE AND (TRANSFORM OR TRANSFECT)
S14          8   RD (unique items)
S15        123   NEUROD1 OR NEUROD2
S16         99   S15 AND TRANSCRIPTION
S17          2   S16 AND BASAL
S18          1   RD (unique items)
? s s16 and glial
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           60600  GLIAL
     S19       4  S16 AND GLIAL
? rd
...completed examining records
     S20       3  RD (unique items)
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 20/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10788975   20323165   PMID: 10862740
  Misexpression of basic helix-loop-helix genes in the murine cerebral
cortex affects cell fate choices and neuronal survival.
  Cai L; Morrow E M; Cepko C L
  Department of Genetics, Howard Hughes Medical Institute, Harvard Medical
School, Boston, Massachusetts 02115, USA.
  Development (Cambridge, England) (ENGLAND) Jul 2000, 127 (14)
 p3021-30, ISSN 0950-1991 Journal Code: 8701744
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  To investigate the role(s) of basic helix-loop-helix genes (bHLH) genes
in the developing murine cerebral cortex, Mash1, Math2, Math3, Neurogenin1
(Ngn1), Ngn2, NeuroD, NeuroD2 and Id1 were transduced in vivo into
the embryonic and postnatal cerebral cortex using retrovirus vectors. The
morphology and location of infected cells were analyzed at postnatal
stages. The data indicate that a subset of bHLH genes are capable of
regulating the choice of neuronal versus glial fate and that, when
misexpressed, they can be deleterious to the survival of differentiating
neurons, but not glia.


 20/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09499910   97413638   PMID: 9270024
  Expression of neurogenic basic helix-loop-helix genes in primitive
neuroectodermal tumors.
  Rostomily R C; Bermingham-McDonogh O; Berger M S; Tapscott S J; Reh T A;
Olson J M
  Department of Neurological Surgery, The University of Washington School
of Medicine, Seattle 98195, USA.
  Cancer research (UNITED STATES) Aug 15 1997, 57 (16) p3526-31,
ISSN 0008-5472 Journal Code: 2984705R
  Contract/Grant No.: NS 30304; NS; NINDS; RO1 NS 28308; NS; NINDS
  Document type: Journal Article
```

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The basic helix-loop-helix (bHLH) class of **transcription** factors plays a pivotal role in tissue-specific determination and differentiation. Moreover, dysregulated expression or loss of function of these factors contributes to leukemogenesis and solid tumor development. Neurogenesis is regulated by genes of the NEUROD/atonal and ACHAETE SCUTE families. We analyzed expression of human **NEUROD1**, **NEUROD2**, NEUROD3, and ACHAETE SCUTE 1 (HASH1) in cerebellar and cerebral primitive neuroectodermal tumors (PNETs), gliomas, and cell lines derived from a variety of neuroectodermal tumors by Northern analysis and in situ hybridization. **NEUROD1** was expressed in each of the 12 medulloblastoma specimens, whereas **NEUROD2** and NEUROD3/neurogenin were expressed in partly overlapping subsets of medulloblastomas. All of the tumors that presented with distant metastases expressed NEUROD3. The only other NEUROD3-positive tumor progressed early in treatment. Human ACHAETE SCUTE homologue (HASH1) was not expressed in medulloblastomas (infratentorial PNETs) but was expressed in three of five supratentorial PNETs. Neuroectodermal tumor cell lines derived from other sites (e.g., neuroblastoma and retinoblastoma) expressed NeuroD and ACHAETE SCUTE family members. No NEUROD message was detected in **glial** tumors or cell lines. Neurogenic bHLH **transcription** factor expression patterns suggest that specific family members may contribute to or reflect biological differences that arise during malignant transformation.

20/3,AB/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13340034 BIOSIS NO.: 200100547183
The bHLH **transcription** factor neurogenin3 is expressed by **glial** restricted precursors and is involved in gliogenesis.
AUTHOR: Lee J C(a); Wu Y(a); Qi Y; Qiu M; Guillemot F P; Rao M S(a)
AUTHOR ADDRESS: (a)Neurobiology and Anatomy, Univ. of Utah, Salt Lake City, UT**USA
JOURNAL: Society for Neuroscience Abstracts 27 (1):p1237 2001
MEDIUM: print
CONFERENCE/MEETING: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001
ISSN: 0190-5295
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: bHLH **transcription** factors have been previously identified as neuronal determination and differentiation factors in the CNS. Recent data suggest that certain bHLH proteins may also function in gliogenesis. For example, overexpression of olig proteins induces the expression of oligodendrocyte-specific markers (Lu et al., 2000; Zhou et al., 2000) while members of the neurogenin family are required for the suppression of the astrocyte lineage (Sun et al., 2001; Nieto et al., 2001). By RT-PCR, we sought to identify bHLH proteins present in **glial** restricted precursor cells (GRPs). In addition to NeuroD and **NeuroD2**, we identified Ngn3 to be expressed by GRPs. Because of its pattern and timing of expression, we investigated whether Ngn3 is involved in gliogenesis. Analysis of the Ngn3 null mouse shows a gradual loss of Nkx2.2 expression in the ventral spinal coral. Previous work has demonstrated that Nkx2.2 is expressed by oligodendrocyte progenitors and that the Nkx2.2 knockout mouse displays a delay and reduction in the appearance of oligodendrocytes (Qi et al., submitted; Soula et al., 2001). Ngn3 can also induce gene expression from the oligodendrocyte-specific PLP promoter. These results suggest that Ngn3 is

involved in gliogenesis. We are currently investigating the specific role of Ngn3 during gliogenesis.

```
 s ash and glial
           22649  ASH
           60600  GLIAL
     S21       0  ASH AND GLIAL
? s ash1
     S22     123  ASH1
? s s22 and transcription
             123  S22
          362053  TRANSCRIPTION
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              71  S23
         3764905  CELL
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              58  S24
          692228  CULTURE
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? t s25/3,ab/all

 25/3,AB/1      (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11232254   21262951   PMID: 11370813
  Differential expression of sympathoadrenal lineage-determining genes and
phenotypic markers in cultured primary neural crest cells.
  Bilodeau M L; Boulineau T; Greulich J D; Hullinger R L; Andrisani O M
  Department of Basic Medical Sciences, Purdue University, West Lafayette,
Indiana 47907-1246, USA.
  In vitro cellular & developmental biology. Animal (United States)  Mar
2001, 37 (3) p185-92, ISSN 1071-2690  Journal Code: 9418515
  Contract/Grant No.: DK 44533; DK; NIDDK
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Bone morphogenetic protein-2 (BMP-2) promotes the development of primary
neural crest cells grown in tissue culture to the sympathoadrenal
(SA) lineage. Independent studies have characterized the expression
patterns of SA-lineage genes in developing chicken embryo; however, studies
using cultured primary neural crest cells have characterized only the
expression patterns of the catecholaminergic markers, tyrosine hydroxylase
(TH) and catecholamines (CAs). To further explore the molecular mechanisms
that control SA-cell development using the in vitro model system, it
is crucial to define the expression patterns of both the catecholaminergic
markers and the genes regulating SA-lineage determination. Accordingly, we
defined, in the absence and presence of BMP-2, the temporal expression
patterns of TH and CA, the SA lineage-determining genes ASH-1, Phox2a, and
Phox2b, the GATA-2 gene, and the pan-neuronal SCG10 gene. Comparison of
these data with the reported temporal and spatial patterns of expression in
vivo demonstrate that the inductive steps of SA-lineage determination,
including the specification of neurotransmitter identity and neuronal fate,
are recapitulated in the neural-crest culture system.
? s epidermal and ash
          117035  EPIDERMAL
           22649  ASH
     S26      65  EPIDERMAL AND ASH
? s s26 and express?
              65  S26
         1578605  EXPRESS?
     S27      13  S26 AND EXPRESS?
? rd
...completed examining records
     S28       8  RD (unique items)
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? t s28/3,ab/all

28/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09441952 97342621 PMID: 9199318
Phosphatidylinositol 4,5-bisphosphate phosphatase regulates the rearrangement of actin filaments.
Sakisaka T; Itoh T; Miura K; Takenawa T
Department of Biochemistry, Institute of Medical Science, University of Tokyo, Minato-ku, Japan.
Molecular and cellular biology (UNITED STATES) Jul 1997, 17 (7) p3841-9, ISSN 0270-7306 Journal Code: 8109087
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Phosphatidylinositol 4,5-bisphosphate (PIP2) reorganizes actin filaments by modulating the functions of a variety of actin-regulatory proteins. Until now, it was thought that bound PIP2 is hydrolyzed only by tyrosine-phosphorylated phospholipase Cgamma (PLCgamma) after the activation of tyrosine kinases. Here, we show a new mechanism for the hydrolysis of bound PIP2 and the regulation of actin filaments by PIP2 phosphatase (synaptojanin). We isolated a 150-kDa protein (p150) from brains that binds the SH3 domains of **Ash**/Grb2. The sequence of this protein was found to be homologous to that of synaptojanin. The **expression** of p150 in COS 7 cells produces a decrease in the number of actin stress fibers in the center of the cells and causes the cells to become multinuclear. On the other hand, the **expression** of a PIP2 phosphatase-negative mutant does not disrupt actin stress fibers or produce the multinuclear phenotype. We have also shown that p150 forms the complexes with **Ash**/Grb2 and **epidermal** growth factor (EGF) receptors only when the cells are treated with EGF and that it reorganizes actin filaments in an EGF-dependent manner. Moreover, the PIP2 phosphatase activity of native p150 purified from bovine brains is not inhibited by profilin, cofilin, or alpha-actinin, although PLCdelta1 activity is markedly inhibited by these proteins. Furthermore, p150 suppresses actin gelation, which is induced by smooth muscle alpha-actinin. All these data suggest that p150 (synaptojanin) hydrolyzes PIP2 bound to actin regulatory proteins, resulting in the rearrangement of actin filaments downstream of tyrosine kinase and **Ash**/Grb2.

28/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08908054 96257761 PMID: 8687411
Interaction of **Ash**/Grb-2 via its SH3 domains with neuron-specific p150 and p65.
Miura K; Miki H; Shimazaki K; Kawai N; Takenawa T
Department of Molecular Oncology, Institute of Medical Science, University of Tokyo, Japan.
Biochemical journal (ENGLAND) Jun 1 1996, 316 (Pt 2) p639-45, ISSN 0264-6021 Journal Code: 2984726R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We found that 180 kDa, 150 kDa (p150), 110 kDa, 100 kDa and 65 kDa (p65) proteins comprise the major **Ash** /Grb-2-binding proteins in bovine brain. Among these proteins, 180 kDa and 100 kDa proteins have already been identified as Sos and dynamin respectively. Here, p150 and p65 were affinity-purified with glutathione S-transferase-**Ash** fusion protein and their partial amino acid sequences were determined. Analysis showed

p150 and p65 to be new proteins. These two proteins bind to both the N-terminal SH3 domain and the C-terminal SH3 domain of **Ash**. It was found that p150 and p65 are **expressed** predominantly in brain, although **Ash** is widely distributed in all tissues examined by Western blots. Immunohistochemical staining of rat brain showed p150 and p65 to be localized in a variety of neurons in the cerebellum and hippocampus, with p65 being especially concentrated in the nerve terminal. When the **Ash** -binding-motif peptide of the **epidermal** growth factor receptor was used to detect complexes formed with **Ash** in vivo, 180 kDa, 150 kDa, 110 kDa, 100 kDa and 65 kDa proteins were also bound; this shows that these proteins form complexes with **Ash** in brain. In addition, p150 and p65 co-immunoprecipitated with **Ash**. All these results suggest that **Ash** may function as a regulator of synaptic vesicle transport through dynamin, p150 and p65.

28/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08620810 95378271 PMID: 7650032
An **epidermal** growth factor receptor-leukocyte tyrosine kinase chimeric receptor generates ligand-dependent growth signals through the Ras signaling pathway.
Ueno H; Hirano N; Kozutsumi H; Sasaki K; Tanaka T; Yazaki Y; Hirai H
Third Department of Internal Medicine, Faculty of Medicine, University of Tokyo, Japan.
Journal of biological chemistry (UNITED STATES) Aug 25 1995, 270 (34) p20135-42, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Leukocyte tyrosine kinase (LTK) is a receptor tyrosine kinase that belongs to the insulin receptor family. LTK is mainly **expressed** in pre B cells and brain. Previously we cloned the full-length cDNA of human LTK, but no ligands have so far been identified, and hence, very little is known about the physiological role of LTK. To analyze the function of the LTK kinase, we constructed chimeric receptors composed of the extracellular domain of **epidermal** growth factor receptor and the transmembrane and the cytoplasmic domains of LTK and established cell lines that stably **express** these chimeric molecules. When cultured in medium containing EGF, growth of these cell lines was stimulated, and these fusion proteins became autophosphorylated and associated with Shc in vivo in a ligand-dependent manner. By treatment with EGF, Shc was associated with the Grb2/**Ash** -Sos complex. Our analyses demonstrate that LTK associates with Grb2/**Ash** through an internal adaptor, Shc, depending on a ligand stimulation. The LTK binding site for Shc was tyrosine 862 at the carboxyl-terminal domain and to a lesser extent tyrosine 485 at the juxtamembrane domain. Both of them are located in NP/AXY motif which is consistent with binding sites for Shc. These findings demonstrate that LTK can activate the Ras pathway in a ligand-dependent manner and that at least one of the functions of this kinase is involved in the cell growth.

28/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08535771 95293763 PMID: 7539782
Tyrosine phosphorylation of the proto-oncogene product Vav and its association with the adapter Grb2/**Ash** in a human leukemia cell line UT-7.
Hanazono Y; Sasaki K; Odai H; Mimura T; Mitani K; Yazaki Y; Hirai H
Third Department of Internal Medicine, Faculty of Medicine, University of Tokyo.

Japanese journal of cancer research : Gann (JAPAN) Apr 1995, 86 (4) p336-41, ISSN 0910-5050 Journal Code: 8509412
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The vav proto-oncogene product (Vav) is **expressed** exclusively in hematopoietic cells and is reported to have guanine nucleotide exchange activity. Here we report that granulocyte-macrophage colony-stimulating factor, interleukin-3, and erythropoietin induce tyrosine phosphorylation of Vav in a human leukemia cell line UT-7. Tyrosine phosphorylation of Vav is rapid and transient; it occurs within 1 min of the stimulation and at physiological concentrations of the factors. Furthermore, we show that Vav is constitutively associated with the adapter molecule Grb2/**Ash** in UT-7. These data suggest that tyrosine kinases, the adapter Grb2/**Ash**, and the guanine nucleotide exchange factor Vav are members of a signaling pathway leading to Ras activation in hematopoietic cells.

28/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07977878 94105125 PMID: 7506413

Epidermal growth factor-receptor mutant lacking the autophosphorylation sites induces phosphorylation of Shc protein and Shc-Grb2/**ASH** association and retains mitogenic activity.

Gotoh N; Tojo A; Muroya K; Hashimoto Y; Hattori S; Nakamura S; Takenawa T ; Yazaki Y; Shibuya M
Department of Genetics, University of Tokyo, Japan.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jan 4 1994, 91 (1) p167-71, ISSN 0027-8424 Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Epidermal growth factor (EGF) receptor (EGFR) can induce cell growth and transformation in a ligand-dependent manner. To examine whether the autophosphorylation of EGFR correlates with the capacity of the activated EGFR to induce cell growth and transformation, we truncated the human EGFR just after residue 1011, removing all three major autophosphorylation sites (DEL1011). Further, a point mutation was introduced at another autophosphorylation site, Tyr-992-->Phe (DEL1011+F992). The wild-type and mutant receptors were stably **expressed** in a NIH 3T3 variant cell line that **expresses** an extremely low level of endogenous EGFR and does not grow with EGF. As expected, DEL1011 and DEL1011+F992 were found to be severely impaired in EGF-induced autophosphorylation, due to the deletion of the appropriate target tyrosines. However, mutant receptors still could induce EGF-dependent DNA synthesis, morphological transformation, and anchorage-independent growth, although the extent of these was significantly reduced when compared with wild-type EGFR. EGF-induced tyrosine phosphorylation of Ras-GTPase activating protein-associated protein p62 and phospholipase C gamma 1 was dramatically reduced in the cells **expressing** DEL1011 and DEL1011+F992. On the other hand, tyrosine phosphorylation of Shc, complex formation of Shc-Grb2/**Ash**, and activation of microtubule-associated protein kinase were still fully induced upon EGF stimulation without binding of Shc or Grb2/**Ash** to the mutant receptor. Thus, tyrosine phosphorylation of Shc may play a crucial role for activating Ras and generating mitotic signals by the activated EGFR mutant.

28/3,AB/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07504075 93028395 PMID: 1384039
Cloning of **ASH**, a ubiquitous protein composed of one Src homology region (SH) 2 and two SH3 domains, from human and rat cDNA libraries.
Matuoka K; Shibata M; Yamakawa A; Takenawa T
Department of Biosignal Research, Tokyo Metropolitan Institute of Gerontology, Japan.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Oct 1 1992, 89 (19) p9015-9, ISSN 0027-8424 Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The protein **ASH** (for abundant Src homology), composed of one Src homology region (SH) 2 and two SH3 domains, was cloned by screening human and rat cDNA libraries with an oligonucleotide probe directed to a consensus sequence of the SH2 domains. The rat-derived **ASH** peptide was comprised of 217 amino acids with a molecular mass of 25-28 kDa and was found to be ubiquitous in rat tissues. A human cDNA clone was also found to code for part of the same protein, suggesting that **ASH** is common to human and rat. The amino acid sequence of **ASH** was strikingly similar to Sem-5, the product of a nematode cell-signaling gene, and **ASH** is most probably a mammalian homologue of Sem-5. **ASH** bound in vitro to phosphotyrosine-containing proteins, including activated **epidermal** growth factor receptor, the **ASH** SH2 domain being responsible for the binding. Induced **expression** of an antisense **ASH** cDNA led to a reduction in cell growth. Considering these observations and the structural homology to Sem-5, **ASH** is likely to function as a ubiquitous signal transducer, possibly resembling Sem-5, which communicates between a receptor protein tyrosine kinase and a Ras protein.

28/3,AB/7 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10907988 BIOSIS NO.: 199799529133
Interactions of the adaptor protein Nck with novel signaling molecules NAP4 and NAP5.
AUTHOR: Matuoka Koozi; Miki Hiroaki; Takahashi Kyoko; Takenawa Tadaomi
AUTHOR ADDRESS: Dep. Biosignal Research, Tokyo Metropolitan Inst. Gerontol., Tokyo 173**Japan
JOURNAL: Cell Structure and Function 21 (6):p607 1996
CONFERENCE/MEETING: Forty-ninth Annual Meeting of the Japan Society for Cell Biology Kyoto, Japan October 23-25, 1996
ISSN: 0386-7196
RECORD TYPE: Citation
LANGUAGE: English
1996

28/3,AB/8 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08958117 BIOSIS NO.: 199396109618
Defecation, apparent absorption, efficiency, and the importance of water obtained in the food for water balance in captive brown long-eared (Plecotus auritus) and Daubenton's (Myotis daubentoni) bats.
AUTHOR: Webb P I; Speakman J R; Racey P A
AUTHOR ADDRESS: Dep. Zool., Univ. Aberdeen, Aberdeen AB9 2TN**UK
JOURNAL: Journal of Zoology (London) 230 (4):p619-628 1993

ISSN: 0952-8369
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Mean apparent dry mass absorption efficiency by P. auritus fed on mealworms was 0.853 (S.D. = O.4, n = 43). Mean apparent energy absorption efficiency by P. auritus and M. daubentoni fed on mealworms was 0.90 (S.D. = 0.007, n = 8). The mean energy content of mealworms was 28.6 kJ cntdot g-1 dry mass (S.D. = 1.1, n = 8), and that of faeces was 19.5 kJ cntdot g-1 (S.D. = 0.7, n = 8) in P. auritus and 19.9 kJ cntdot g-1 (S. D. = 1.3, n = 8) in P. daubentoni. Water content of mealworms was 61.1% wet mass (S.D. = 1.4, n = 173); water content of faeces was 73.3% in P. auritus (S.D. = 6.8, n=76) and 72.3% (S.D.=7.0, n=42) in M. daubentoni. Oven-dried mealworms consisted of lt 1% **ash**, lt 1% carbohydrate, 31% lipid and 39% protein. We suggest that the dry mass unaccounted for (28%) represented chitin, of which 59% was apparently absorbed during digestion. Apparent absorption by mass of both lipid and protein by P. auritus fed on mealworms was greater than 90%. Cumulative postprandial defecation was sigmoidal in both bat species with 50% (by mass) of faeces being voided within 4 h and 95% within 12 h of feeding. On the basis of previous measurements, using doubly-labelled water, of daily energy expenditure and water flux in free-living P. auritus, we predict that water intake via the food, as free water and as potential metabolic water, represents 20 to 40% of total daily water flux for P. auritus during lactation in the wild.

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s src and glial
          23164  SRC
          60600  GLIAL
     S29    105  SRC AND GLIAL
? s s29 and grb2
            105  S29
           2974  GRB2
     S30      4  S29 AND GRB2
? rd
...completed examining records
     S31      4  RD (unique items)
? t s31/3,ab/all

 31/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13799556   22227288   PMID: 12242309
  The neuron-specific Rai (ShcC) adaptor protein inhibits apoptosis by
coupling Ret to the phosphatidylinositol 3-kinase/Akt signaling pathway.
  Pelicci Giuliana; Troglio Flavia; Bodini Alessandra; Melillo Rosa Marina;
Pettirossi Valentina; Coda Laura; De Giuseppe Antonio; Santoro Massimo;
Pelicci Pier Giuseppe
  Department of Experimental Oncology, European Institute of Oncology,
20141 Milan, Italy. pgpelicci@ieo.it
  Molecular and cellular biology (United States) Oct 2002, 22 (20)
 p7351-63, ISSN 0270-7306 Journal Code: 8109087
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Rai is a recently identified member of the family of Shc-like proteins,
which are cytoplasmic signal transducers characterized by the unique
PTB-CH1-SH2 modular organization. Rai expression is restricted to neuronal
cells and regulates in vivo the number of postmitotic sympathetic neurons.
We report here that Rai is not a common substrate of receptor tyrosine
kinases under physiological conditions and that among the analyzed
receptors (Ret, epidermal growth factor receptor, and TrkA) it is activated
specifically by Ret. Overexpression of Rai in neuronal cell lines promoted
survival by reducing apoptosis both under conditions of limited
availability of the Ret ligand glial cell line-derived neurotrophic
factor (GDNF) and in the absence of Ret activation. Overexpressed Rai
resulted in the potentiation of the Ret-dependent activation of
phosphatidylinositol 3-kinase (PI3K) and Akt. Notably, increased Akt
phosphorylation and PI3K activity were also found under basal conditions,
e.g., in serum-starved neuronal cells. Phosphorylated and
hypophosphorylated Rai proteins form a constitutive complex with the p85
subunit of PI3K: upon Ret triggering, the Rai-PI3K complex is recruited to
the tyrosine-phosphorylated Ret receptor through the binding of the Rai PTB
domain to tyrosine 1062 of Ret. In neurons treated with low concentrations
of GDNF, the prosurvival effect of Rai depends on Rai phosphorylation and
Ret activation. In the absence of Ret activation, the prosurvival effect of
Rai is, instead, phosphorylation independent. Finally, we showed that
overexpression of Rai, at variance with Shc, had no effects on the early
peak of mitogen-activated protein kinase (MAPK) activation, whereas it
increased its activation at later time points. Phosphorylated Rai, however,
was not found in complexes with Grb2. We propose that Rai potentiates
the MAPK and PI3K signaling pathways and regulates Ret-dependent and
-independent survival signals.


 31/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09989497   98435847   PMID: 9764818
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Grb2 binding to the different isoforms of Ret tyrosine kinase.
Alberti L; Borrello M G; Ghizzoni S; Torriti F; Rizzetti M G; Pierotti M A
Division of Experimental Oncology A, Istituto Nazionale Tumori, Milan, Italy.
Oncogene (ENGLAND) Sep 3 1998, 17 (9) p1079-87, ISSN 0950-9232 Journal Code: 8711562
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The RET proto-oncogene encodes two isoforms of a receptor tyrosine kinase which plays a role in neural crest and kidney development. Ret ligands have been recently identified as the neuron survival factor GDNF (**Glial** -Derived Neurotrophic Factor) and Neurturin. Somatic rearrangements of RET, designated RET/PTCs, have been frequently detected in papillary thyroid carcinomas. In addition, distinct germ-line mutations of RET gene have been associated with the inherited cancer syndromes MEN (Multiple Endocrine Neoplasia) 2A, 2B and FMTC (Familial Medullar Thyroid Carcinomas) as well as with the congenital megacolon or Hirschsprung's disease, thus enlightening a significant role of this receptor gene in diverse human pathologic conditions. In this study, by performing classical inhibition experiments using synthetic phosphopeptides and by site-directed mutagenesis of the putative docking site, we have determined that for **Grb2** the latter is provided by the tyrosine 620 of Ret/ptc2 long isoform (corresponding to Tyr 1096 on proto-Ret). However, in intact cells, the interaction of **Grb2** with the two short and long Ret isoforms expressed separately is of similar strength, thus suggesting that Ret short isoform interaction with **Grb2** could be mediated not only by Shc but also by a molecule that binds preferentially to this isoform. This possibility is supported by the evidence that the mutant Ret/ptc2Y620F long isoform displays a weak coimmunoprecipitation with **Grb2** and that this mutant, lacking the docking site for **Grb2** but owing all the others phosphotyrosines, surprisingly displays a reduced transforming activity compared to that of the two WTs oncogenes. We thus conclude that in intact cells both Ret isoforms bind to **Grb2** , although with different modalities. In addition, the present results are in agreement with the possibility that different signal transduction pathways are associated with the two isoforms of Ret.

31/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09543267 97445110 PMID: 9299438
Characterization of Ret-Shc-**Grb2** complex induced by GDNF, MEN 2A, and MEN 2B mutations.
Ohiwa M; Murakami H; Iwashita T; Asai N; Iwata Y; Imai T; Funahashi H; Takagi H; Takahashi M
Department of Pathology, Nagoya University School of Medicine, Japan.
Biochemical and biophysical research communications (UNITED STATES) Aug 28 1997, 237 (3) p747-51, ISSN 0006-291X Journal Code: 0372516
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We analyzed the intracellular signalling pathway through Ret activated by **glial** -cell-line-derived neurotrophic factor (GDNF), multiple endocrine neoplasia (MEN) 2A and 2B mutations. The results showed that all of them induce a signal transducing complex consisting of Ret, Shc, and **Grb2** proteins. In addition, GDNF clearly activated a Ras-MAPK pathway in human neuroblastoma cells. Rat is expressed mainly as two isoforms that differ in the carboxy-terminal sequence: a long isoform (1114 amino acids) and a short isoform (1072 amino acids). The long isoform contains the

consensus sequence for binding of the Shc PTB domain but not of its SH2 domain, whereas the short isoform has the consensus sequences for binding of both domains. In vitro binding assay revealed that the long isoform of the MEN2A-Ret protein and both isoforms of the MEN2B-Ret protein bound preferentially to the Shc PTB domain. On the other hand, the short isoform of MEN2A-Ret bound to the PTB and SH2 domains. In neuroblastoma cells expressing both isoforms of Ret, its activation by GDNF also resulted in the binding of both domains. GDNF and MEN 2A mutations activate Ret by inducing its dimerization, whereas the MEN 2B mutation increases Ret catalytic activity without dimerization. Our results thus suggest that Ret dimerization might be required for binding of the Shc SH2 domain to the short isoform.

31/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08821349 96170040 PMID: 8596638
A **Grb2** -associated docking protein in EGF- and insulin-receptor signalling.
Holgado-Madruga M; Emlet D R; Moscatello D K; Godwin A K; Wong A J
Department of Microbiology & Immunology, Jefferson Cancer Institute, Philadelphia, Pennsylvania 19107, USA.
Nature (ENGLAND) Feb 8 1996, 379 (6565) p560-4, ISSN 0028-0836 Journal Code: 0410462
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The protein **Grb2** plays a central role in signalling by receptor protein-tyrosine kinases, where its SH2 domain binds to the receptor and its two SH3 domains link to effectors. One target effector is Sos, so **Grb2** links receptor protein-tyrosine kinases with the Ras signalling pathway. The SH3 domains can also couple to other signalling proteins, including Vav, c-Abl and dynamin. We have identified several bands in **glial** and medulloblastoma tumours that are recognized by **Grb2** but these did not correspond to any known protein. Here we use recombinant **Grb2** to isolate a complementary DNA called Gab1 (for **Grb2** -associated binder-1). Gab1 shares amino-acid homology and several structural features with IRS-1 (insulin-receptor substrate-1; refs 6,7), is a substrate of the EGF and insulin receptors, and can act as a docking protein for several SH2-containing proteins. Over-expression of Gab1 enhances cell growth and results in transformation. We conclude that Gab1 is a new protein in EGF and insulin receptor signalling which could integrate signals from different systems.

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 s zic and glial
            106  ZIC
          60600  GLIAL
     S32      3  ZIC AND GLIAL
? rd
...completed examining records
     S33      2  RD (unique items)
? t s33/3,ab/all

 33/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11101906   21125744   PMID: 11038359
  Transcription factors Zic1 and Zic2 bind and transactivate the
apolipoprotein E gene promoter.
  Salero E; Perez-Sen R; Aruga J; Gimenez C; Zafra F
  Centro de Biologia Molecular Severo Ochoa, Facultad de Ciencias,
Universidad Autonoma de Madrid-Consejo Superior de Investigaciones
Cientificas, 28049 Madrid, Spain.
  Journal of biological chemistry (United States)  Jan 19 2001,  276  (3)
 p1881-8,  ISSN 0021-9258  Journal Code: 2985121R
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  We have used the yeast one-hybrid system to identify transcription
factors that bind to specific sequences in proximal regions of the
apolipoprotein E gene promoter. The sequence between -163 and -124, that
has been previously defined as a functional promoter element, was used as a
bait to screen a human brain cDNA library. Ten cDNA clones that encoded
portions of the human Zic1 (five clones) and Zic2 (five clones)
transcription factors were isolated. Electrophoretic mobility shift assays
confirmed the presence of a binding site for Zic1 and Zic2 in the -136/-125
region. Displacement of binding with oligonucleotides derived from adjacent
sequences within the APOE promoter revealed the existence of two additional
Zic -binding sequences in this promoter. These sequences were
identified by electrophoretic mobility shift assays and mutational analysis
in regions -65/-54 and -185/-174. Cotransfection of Zic1 and Zic2
expression vector and different APOE promoter-luciferase reporter
constructs in U87 glioblastoma cell line showed that the three binding
sites partially contributed to the trans-stimulation of the luciferase
reporter. Ectopic expression of Zic1 and Zic2 in U87 cells also
trans-stimulated the expression of the endogenous gene, increasing the
amount of apolipoprotein E produced by glial cells. These data
indicate that Zic proteins might contribute to the transcriptional
activity of the apolipoprotein E gene and suggest that apolipoprotein E
could mediate some of the developmental processes in which Zic
 proteins are involved.


 33/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10110729   99095534   PMID: 9879461
  Medulloblastoma in an adult suggestive of external granule cells as its
origin: a histological and immunohistochemical study.
  Miyata H; Ikawa E; Ohama E
  Division of Neuropathology, Faculty of Medicine, Tottori University,
Japan. hajime@grape.med.tottori-u.ac.jp
  Brain tumor pathology (JAPAN)  1998,  15  (1)  p31-5,  ISSN 1433-7398
Journal Code: 9716507
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
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Record type: Completed

We describe a rare case of medulloblastoma in an adult woman with histological findings suggesting an origin for this neoplasm in the external granular layer or its remnants. The patient presented with cerebellar dysfunction, and neuroimaging revealed a right cerebellar mass lesion. Pathological examination of the operative specimen revealed a medulloblastoma with occasional areas of neuronal or **glial** differentiation. **Zic** protein was also detected immunohistochemically in the tumor cells. The tumor cells were mainly distributed in the subarachnoid space and extended to the cerebellar parenchyma through the perivascular space to form tumor nodules. A suggestive finding, as concerns the origin of this neoplasm, was that the tumor cells were also spread evenly along the subpial zone of the molecular layer, reminiscent of the cellular architecture of the fetal external granular layer.

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? s myt1
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              108  S34
            60600  GLIAL
     S35        5  S34 AND GLIAL
? rd
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 36/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09632596   98038874   PMID: 9373037
   Myelin transcription factor 1 (Myt1 ) of the oligodendrocyte
lineage, along with a closely related CCHC zinc finger, is expressed in
developing neurons in the mammalian central nervous system.
  Kim J G; Armstrong R C; v Agoston D; Robinsky A; Wiese C; Nagle J; Hudson
L D
  Laboratory of Developmental Neurogenetics, National Institute of
Neurological Disorders and Stroke, National Institutes of Health, Bethesda,
Maryland 20892-4160, USA.
  Journal of neuroscience research (UNITED STATES) Oct 15 1997, 50 (2)
 p272-90, ISSN 0360-4012 Journal Code: 7600111
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  The establishment and operation of the nervous system requires genetic
regulation by a network of DNA-binding proteins, among which is the zinc
finger superfamily of transcription factors. We have cloned and
characterized a member of the unusual Cys-Cys-His-Cys (also referred to as
Cys2HisCys, CCHC, or C2HC) class of zinc finger proteins in the developing
nervous system. The novel gene, Myt1 -like (Myt1l), is highly
homologous to the original representative of this class, Myelin
transcription factor 1 (Myt1) (Kim and Hudson, 1992). The MYT1
gene maps to human chromosome 20, while MYT1L maps to a region of human
chromosome 2. Both zinc finger proteins are found in neurons at early
stages of differentiation, with germinal zone cells displaying intense
staining for MyT1. Unlike Myt1, Myt1l has not been detected in
the glial lineage. Neurons that express Myt1l also express TuJ1,
which marks neurons around the period of terminal mitosis. The Myt1l
protein resides in distinct domains within the neuronal nucleus, analogous
to the discrete pattern previously noted for Myt1 (Armstrong et al.:
14:303-321, 1995). The developmental expression and localization of these
two multifingered CCHC proteins suggests that each may play a role in the
development of neurons and oligodendroglia in the mammalian central nervous
system.


 36/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09448117   97354646   PMID: 9210873
  High-grade human brain tumors exhibit increased expression of myelin
transcription factor 1 (MYT1), a zinc finger DNA-binding protein.
  Armstrong R C; Migneault A; Shegog M L; Kim J G; Hudson L D; Hessler R B
  Department of Anatomy and Cell Biology, Uniformed Services University of
the Health Sciences, Bethesda, MD 20814-4799, USA.
  Journal of neuropathology and experimental neurology (UNITED STATES)
Jul 1997, 56 (7) p772-81, ISSN 0022-3069 Journal Code: 2985192R
  Contract/Grant No.: NO1-HD-1-3138; HD; NICHD; NS33316; NS; NINDS
  Document type: Journal Article
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Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Detection and characterization of distinct central nervous system (CNS) tumor cell types is clinically important since distinct tumor types are associated with different prognoses and treatments. However, there is currently a lack of markers to identify certain glioma types and insufficient understanding as to which cells give rise to different glioma cell types. In the present study, biopsy specimens from human brain tumors were analyzed for expression of Myelin Transcription Factor 1 (**MYT1**) to explore the extent to which glioma cells reflect characteristic expression of **MYT1** in developing **glial** progenitor cells. Immunostaining with an antibody against **MYT1** revealed widespread immunoreactivity that was most prominent in high-grade oligodendrogliomas, astrocytomas, and mixed oligoastrocytomas as well as in a dysembryoplastic neuroepithelial tumor. **MYT1** immunoreactivity in tumor regions generally correlated with the prevalence of cells exhibiting nuclear immunolabeling with an antibody against Ki-67, suggesting an association of **MYT1** with cell proliferation that was also observed in normal adult human and rat brain in the germinal subependymal zone. The **MYT1** immunoreactivity was frequently nuclear, appearing as dotted or punctate, but in some cases it was localized to the cytoplasm. In combination with histopathological studies and analysis of Ki-67 immunoreactivity, examination of **MYT1** immunolabeling may provide additional information to aid in the detection and diagnosis of CNS tumors.

36/3,AB/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11409847 BIOSIS NO.: 199800191179
Transcription factors that set the stage for neuronal and **glial** differentiation.
AUTHOR: Hudson Lynn D(a)
AUTHOR ADDRESS: (a)Lab. Dev. Neurogenetics, NINDS, NIH, Bethesda, MD 20892-4160**USA
JOURNAL: Journal of Neurochemistry 70 (SUPPL. 1):pS41 1998
CONFERENCE/MEETING: 29th Annual Meeting of the American Society for Neurochemistry Denver, Colorado, USA March 7-11, 1998
SPONSOR: American Society for Neurochemistry
ISSN: 0022-3042
RECORD TYPE: Citation
LANGUAGE: English
1998